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The Newer Concepts of Meat in Nutrition

Meat...

and its Contribution to Basic Nutritional Needs

IN THE nutritional evaluation of a given food, experimental conditions usually are deliberately adjusted so as to highlight the biologic properties of only one constituent of the food under study. In consequence, undue emphasis may be placed upon one contained nutrient to the exclusion or detriment of all others, thereby leading to unfavorable and otherwise incorrect comparisons.

In the case of meat, its nutritional advantages must be evaluated in the light of its total complex composition, and not on the basis of its protein or mineral or vitamin content alone. Meat makes a well-rounded contribution to the human dietary. It provides not only one, but several nutritional essentials, hence no food should be weighed against it solely on the basis of one constituent.

Although meat is man's acknowledged primary source of biologically complete protein, it is more than merely a purveyor of essential amino acids. Its extractives, tasty and stimulating to the digestive juices, whet the appetite and enhance the digestive processes. Meat is a rich source of iron, and is a potent weapon in preventing the nutritional anemia so often observed in both children and adults subsisting on a meat free or meat poor diet. Meat also supplies the copper necessary for iron utilization, and provides generously of phosphorus. Not all protein containing foods—good as they are—supply these essential minerals.

Meat is also an excellent source of the B vitamins thiamine, riboflavin, and niacin. Its vitamin content is at least as great as that of many other excellent foods which are deficient in the other nutrients supplied by meat.

Thus meat becomes one of the most important constituents of the wartime dietary, since its rich supply of varied essential nutrients complements and enhances the nutritional value of the more available, non-rationed foodstuffs. Its inclusion in the dietary in the full amounts now permitted by regulations assures a sustaining, nutritionally adequate dietary.

ACCEPTED AMERICAN MEDICAL ASSN Council on Foods

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American Meat Institute
CHICAGO

SURGERY
GYNECOLOGY AND OBSTETRICS
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INTRAVENOUS HUMAN PLASMA AND SERUM THERAPY

The Cause of Reactions with Particular Reference to the Use of Concentrated Plasma and Serum

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THE remarkably low rate of reactions following the intravenous administration of properly prepared human plasma and serum has been one of the most important factors in the rapid development of this form of therapy. Many workers having extensive experience with normal plasma (29, 53) normal serum (27, 28) and dilute plasma (10) have reported such a low percentage of ill effects from the intravenous use of these solutions as to establish a degree of safety equal to or even surpassing other medications commonly given by veins. However, it has not been generally appreciated that concentrated plasma or serum may be administered by the same route with equal safety and in the opinion of the authors, with superior therapeutic effectiveness.

The advantages of concentrated plasma and serum as observed in the William Buchanan Plasma Center have been described and consistently advocated during the past 3 years in several reports (14, 18, 19, 35). In particular, the small package and the increased speed and simplicity of use of dried plasma packaged for administration in concentrated form have been held to be of particular significance for military use (13, 15, 16). Accordingly it seems worth while to present a study of reactions based on extensive observations in the preparation and administration of concentrated plasma in order to do away with misconceptions concerning the safety of this type of therapy and to establish confidence in its use. In addition, it seems likely that the percentage of ill effects in patients following plasma therapy in general can be even further reduced by a greater understanding of the factors causing untoward manifestations.

Such factors may be related to any form of plasma or serum solutions, whether it be dilute (protein concentration, 3 to 4 grams per cent), normal (protein concentration, 5 to 7 grams per cent), or the concentrated form (protein concentration, 15 to 24 grams per cent). Since concentration of plasma will also concentrate any injurious agents present, care must be exercised so that the recipient is not adversely affected by the greater quantity of dissolved material that could be given per unit of time than with less concentrated solutions (normal or dilute).

We must point out, of course, that the observations made and conclusions drawn deal

From the William Buchanan Blood, Plasma, and Serum Center of Baylor University Hospital, Dallas, Texas.

only with concentrated plasma prepared as previously outlined (13, 15, 16). The salient features of these methods are: (1) pyrogen free technique for preparation of all apparatus, tubing and solutions; (2) sterile techniques throughout, checked by bacteriologic control studies; (3) pooling of blood of all different types just prior to separation of plasma; (4) bulk desiccation of plasma from the frozen state by the adtevac process; (5) sterile transference of dry plasma to small final container.

In this study the various causes of reactions are considered in relation to four major possibilities: (1) factors inherent in the plasma or serum before preparation (related to donor); (2) factors introduced into the plasma during the preparation (related to processing); (3) peculiarities or idiosyncrasies of the patient (related to the recipient); (4) faults in administration (related to indications, contraindications, and mode of administration).

Pyrogenic or chill-fever reactions. The most common type of reaction, the pyrogenic or chill-fever reaction, is related principally to preparation, although the recipient must also be considered, because sensitivity to the factors causing this type of response varies from individual to individual.

The typical pyrogenic reaction is characterized by a chill beginning 30 minutes to 1 hour after the injection, followed by a sharp rise in body temperature of 2 to 5 degrees F. (see Fig. 2). The fever, subsiding rapidly is usually back to the prereaction level in 3 to 4 hours. The patient may experience backache, headache, apprehension and anxiety, and may vomit. There are milder types of such reactions with or without chills, with lower temperature elevations, and with or without subjective manifestations. In exceedingly rare cases, the reaction may be very severe with persistent hyperpyrexia and terminally a shock-like state resulting in death. We have never encountered this malignant reaction following plasma or serum therapy.

The agents responsible for these reactions termed pyrogenic substances, or pyrogens, are produced in water by the growth of several bacteria. As early as 1911, Wechselmann, and Hort and Penfold pointed out that febrile reactions were due to contamination of distilled water used in preparing intravenous injections. These observations were somewhat neglected but the work of Seibert and co-workers (16, 21, 45, 57) put the concept of pyrogens on a firm basis. Since that time many observers (Titus and Dodds; Rademaker; Perkins; Milbert; Banks; Nelson; Co Tui and co-workers, and Walter) have reached similar conclusions.

Present knowledge of pyrogens may be summarized briefly: These bacterial products (and possibly other protein or protein-like substances) cannot be destroyed by the ordinary autoclaving technique unless prolonged over 7 hours or much higher temperatures are employed. Proper distillation in special spray proof stills (41) is the most practical and commonly used method for obtaining pyrogen-free water. Pyrogens may also be removed by adsorption with charcoal, sufficient filtration through Seitz packs, or by passing the water through a 200 second Zsigmondy membrane filter (6).

Pyrogens are exceedingly soluble and if present on a surface (rubber tube, syringe, or other equipment) they will be readily dissolved by water running over these surfaces. The dose required to produce a reaction is small but varies as there appears to be a variable individual susceptibility to a given dose of pyrogens (11).

The plasma and serum service at Baylor University Hospital (William Buchanan Center) presents an opportunity for a comprehensive survey of reactions because it has been almost entirely a concentrated plasma and serum service since its inception 3 years ago. Due to satisfactory clinical and experimental results following the use of these concentrated solutions and because of the co-operation and enthusiasm of the practicing physicians of Dallas and vicinity, a great deal of information concerning the use of concentrated plasma and serum has been obtained during these 3 years.

In our analysis of reactions related to these concentrated solutions it should be noted that these injections varied from 50 to 300 cubic centimeters as single doses; however, 50 to 100 cubic centimeters of concentrate given in

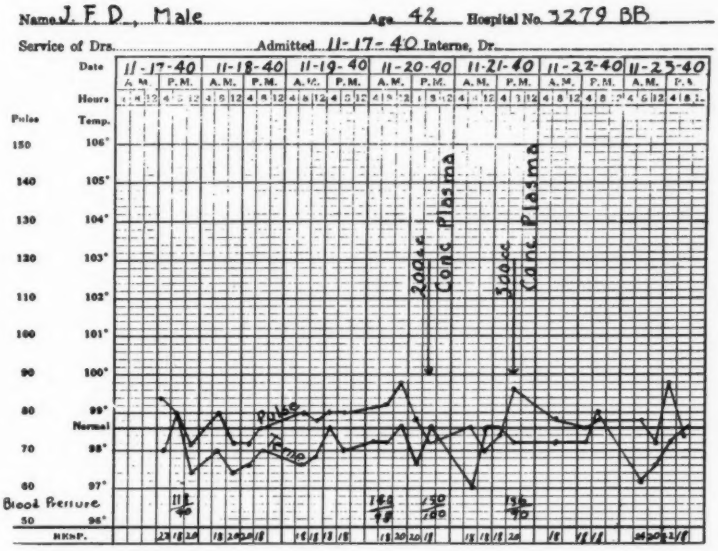

Fig. 1. Diagnosis: glomerulonephritis with nephrotic syndrome. This case demonstrates the appearance of temperature and pulse chart when no reaction occurs. Notice no change in these two curves following the concentrated plasma injections as compared to the same curves on the days before and after the injections. There was slight hypertension which was not altered by the injections. The plasma was given to encourage diuresis, 200 and 300 cubic centimeters of the concentrate as separate single doses.

1 to 15 minutes' time constituted the usual single dose. During the 3 years' period of study plasma concentrations varied somewhat with plasma proteins ranging from 15 to 24 grams per cent. Such doses are equivalent to 200 to 400 cubic centimeters of normal plasma. With this rapid injection of a concentrated solution an innocuous product is more necessary than when more dilute solutions are given. It is also true that a low reaction rate in relation to concentrated plasma can be taken to represent strong evidence supporting the method of preparation of the product. We also believe that information regarding these solutions may be applied to the entire plasma and serum field.

The reaction study includes only the patients in Baylor Hospital who received concentrated plasma or serum although it is estimated that a larger number of patients received such plasma through our state wide service. It was thus possible for one of us (E. E. M.) to check each chart of 520 patients receiving 1,160 separate injections of concentrated plasma or serum, in an attempt to standardize the appraisals of the reactions as much as it was possible.

Information concerning the age, sex, diagnosis, number of injections, total amount given and ill effects resulting from the injections was recorded on each case. The temperatures, pulse, and respiration before and after the injection were checked. An elevation in the fever curve shortly after the injection up to 1 to 2 hours, was considered a reaction, except when the temperature change conformed exactly with temperature changes on the days before the injection (see Figures 1, 2, 3, 4). The febrile and urticarial reaction rates are presented in Table I.

TABLE I.—FEBRILE AND URTICARIAL REACTION RATES—1,160 INJECTIONS—520 CASES

Type	Number	Percentage
Pyrogenic	14	1.2
Questionable pyrogenic	4	0.344
Total pyrogenic	18	1.55
Urticarial	6	0.51
Total pyrogenic and urticarial	24	2.06

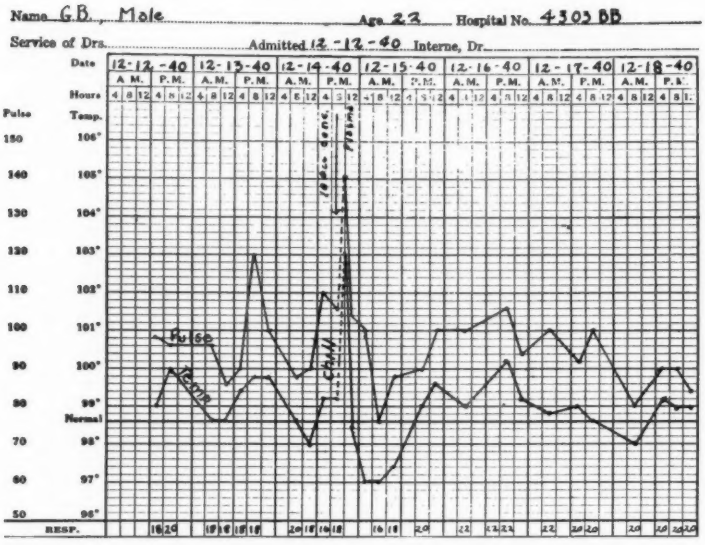

Fig. 2 Diagnosis: second degree burns, left arm, neck, and chest. This case demonstrates a typical pyrogenic reaction following concentrated plasma. Notice the sudden effects. The reaction began with a severe headache, "aching in the bones," generalized malaise immediately after the injection. One hour and forty-five minutes later the temperature was elevated from 99.6 to 103 degrees F. and the pulse rate went to 140 beats per minute from a previous level of 106. There was a severe chill 1 hour after the administration. Five hours after the injection the temperature was 98.4 degrees and the pulse rate 104. This was followed by a short period of subnormal temperature and then complete recovery. Notice that the temperature and pulse curves are approximately the same on the days before and after the reaction.

The 14 typical evanescent *pyrogenic reactions* gives a reaction rate of 1.2 per cent. In 2 cases of this group, just before the plasma was injected, the patient received 1000 cubic centimeters of saline solution. Which of the two solutions caused the reaction could not be determined, so both reactions were included in the plasma group. In 4 other instances the temperature elevation following concentrated plasma was greater than the usual elevations for that day, but conformed well with the previous diurnal temperature changes. These 4 responses have been termed questionable pyrogenic reactions (0.34 per cent). This makes an overall total of 1.55 per cent for the incidence of pyrogenic reactions.

There are many reasons to believe that the main cause of these few reactions resided in the water used to dissolve the plasma and in 1 case sterile but not pyrogen free water was used by mistake to dissolve the plasma. This idea is also supported by the fact that wide fluctuations have occurred in the whole blood transfusion service, apparently related to variations in the preparation of the distilled water and its use in preparing equipment. Nevertheless, the concentrated plasma febrile reaction rate (1.55 per cent) is significantly lower than that of the blood transfusion service (5.18 per cent in 2,139 transfusions during the year November, 1941, to November, 1942). Furthermore our belief that water was responsible for the reactions is supported by the fact that at Jefferson Medical College, where adtevac plasma is being given in concentrated solution, Jones and co-workers (24) have observed only 3 reactions in 1,600 injections of concentrated plasma. Since our reaction study includes the entire period of concentrated plasma production at Baylor Hospital from the inception of the service, it includes the development periods when operations were at

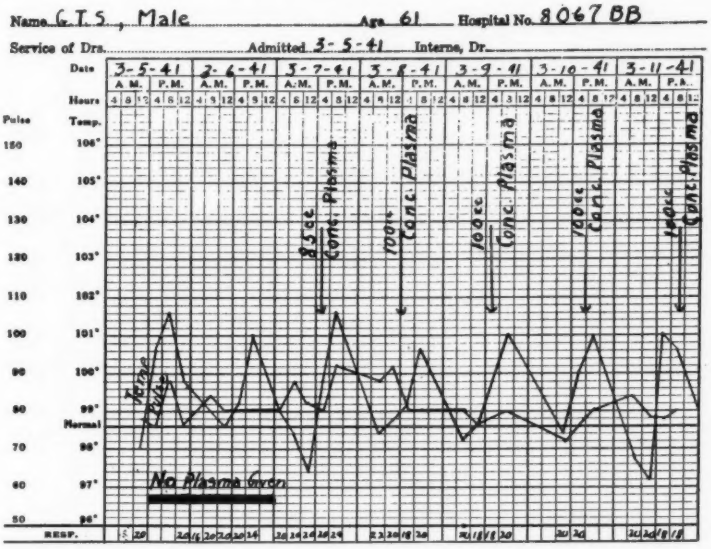

Fig. 3. Diagnosis: carcinoma of colon with metastasis to liver, hypoproteinemia. This case is presented in order to point out that elevations of the temperature (upper curve with daily peaks) following concentrated plasma which conform exactly in time of occurrence and degree with previous temperature changes do not represent reactions. This patient had an elevation of the temperature to 101 degrees F. each evening, invariably demonstrated at 7:30 p.m. The same temperature changes occurred on the 2 days before therapy was started. Notice that on the last dose presented (March 11, 1941) the same temperature elevation occurred before the plasma was given. There were no changes in the pulse rate, no subjective complaints as observed in the pyrogenic type of reaction; therefore, these changes are considered unrelated to the therapy and no reactions were recorded in this case.

times conducted under adverse circumstances. With present equipment and technique, we have reason to believe the present and future reaction rate will be considerably less than the overall rate of 1.55 per cent.

It should be possible to eradicate the pyrogenic type of reaction with the use of a proper pyrogen-free technique from the time the blood is collected to the preparation of the water and equipment used in dissolving the dry product. In order to assure an entirely pyrogen-free plasma solvent, we have lately added a step in its preparation. The water is distilled by a Barnstead type Q still, filter cell added, and the water immediately filtered through several Seitz pads and finally through a Mandler candle to remove any asbestos particles that remain. From the final filtration reservoir it is dispensed in bottles and immediately autoclaved.

Urticarial reactions are a type of allergic manifestation, characterized by itching, erythema, and multiple wheals of the skin. In severe cases edema of eyelids and lips may develop. The reaction appears immediately after the injection, usually generalized over the body. These reactions may be classified as related to factors inherent in the donor's blood and to peculiarities of the recipient.

As shown in Table I, 6 urticarial reactions have been observed in 1,160 injections, representing a rate of 0.517 per cent. This compares with a rate of 1.6 per cent for whole blood transfusions during the period between November, 1941, to November, 1942, involving 2,139 transfusions. This difference in favor of plasma appears significant in view of the large number of injections involved. The smaller urticarial rate for plasma may be ascribed to dilution of allergens in a given blood sample

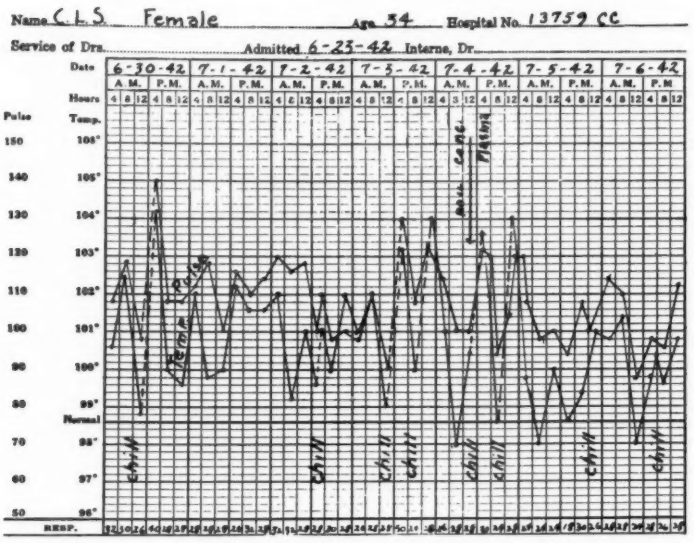

Fig. 4. Diagnosis: fecal fistula following operation for intestinal obstruction. This case is similar to that shown in Figure 3 in that the changes in the temperature and pulse curves following concentrated plasma were not considered as reactions. Notice that the patient had exactly the same disturbances in the pulse and temperature, at the same time of day on the day previous to the injection. Also the patient had several chills with fever before this time and even a day after the injection. There are not many cases of this type in our series, so that even if they were included as reaction, the rate would not be substantially altered.

through its dilution in the stage of pooling of blood. It also indicates that the methods of processing employed did not cause changes or add substances responsible for this type of reaction.

Only 2 of the urticarial reactions were severe. The first consisted of a generalized pruritis 12 minutes after 150 cubic centimeters of concentrated plasma, followed by wheals, edema of eyelids, transient increase in respiratory rate, and much discomfort and anxiety (see Fig. 5). The second severe reaction followed a 50 cubic centimeter dose in an emaciated 8 year old child with peritonitis. Six similar doses previously given were uneventful. The eighth dose given more slowly produced mild urticaria. Thereafter, 4 doses given in normal or dilute form gave no reactions. Neither patient showed change in the temperature curve and both recovered completely.

The most peculiar reaction of urticarial type showed a narrow zone of wheals and smarting of the skin over the right median cephalic vein from the level of injection of concentrated serum to the point where the vein passes beneath the deltoid muscle. This patient experienced no other allergic manifestations.

No lasting complications have occurred even with the severe urticarial reactions and rapid relief after hypodermic administration of 0.3 to 0.5 cubic centimeter of epinephrin solution 1:1000 was the rule.

Prevention of this type of reaction seems difficult because we cannot foretell which patients will be sensitive. Skin testing has not been satisfactory in our experience. Collection from donors in the fasting state has been suggested. This practice has not been followed in this center because of practical difficulties in taking donors from all sections of Texas. The use of large blood pools (25 to 50 pints) may help by dilution of allergen-containing blood; however, since urticarial manifestations following concentrated human plasma,

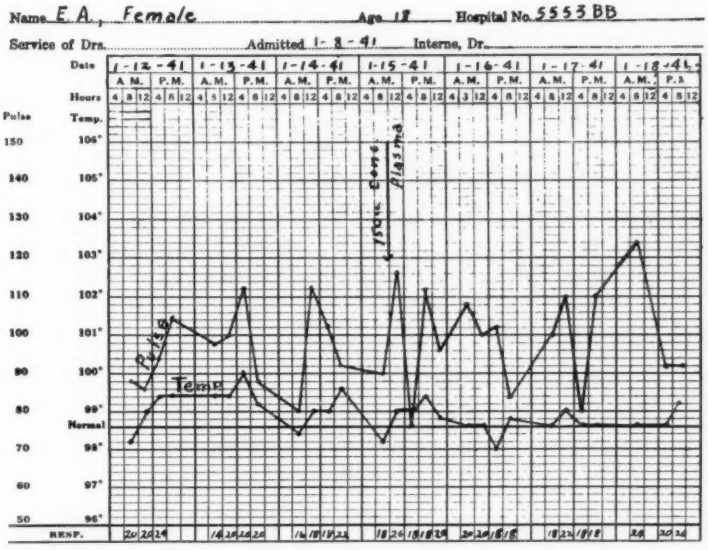

Fig. 5. Diagnosis: diabetes mellitus. This case is mentioned in the text. There was a severe urticarial reaction following 150 cubic centimeters of concentrated plasma as a single dose. Notice no change in the temperature curve as compared to that of the previous 2 days. There was a transient drop in the pulse rate but such changes occurred frequently in this case on other days. The respirations were transiently increased. The main changes were transient and related to the skin.

as shown in this study, are unaccompanied by lasting or other serious results, they do not appear to be a serious objection to the use of plasma, concentrated or otherwise.

Citrate reactions. A type of reaction which has been extremely rare in the clinical use of concentrated plasma but which seems to be of marked importance in animal experimentation is the citrate reaction. As we have previously indicated (18, 34) this type of response is due to the binding of calcium by the excess of sodium citrate in the anticoagulant solution into which the blood is collected initially. The fully developed reaction is characterized by generalized tingling sensations, apprehension, dilation of pupils, carpopedal spasm, and tetany. Chvostek's sign is positive and there is general rigidity. Cyanosis was seen in 3 reactions and a transient apnea in a newborn infant.

This type of reaction is related to three factors, processing (addition of citrate), mode of administration (rapid injection) and peculiarities of recipient (low blood calcium of infants and hypocalcemic adults). The sodium citrate added during blood collection must be slightly in excess in order to assure complete binding of calcium as relatively un-ionized calcium citrate to prevent coagulation. When the plasma is given as a concentrated solution, the citrate also is concentrated. This means that more sodium citrate can be given per unit of time than is the case with normal or dilute plasma. The speed with which citrate is given is very important in its relation to reactions, because citrate is very rapidly oxidized after entering the blood stream (43, 48). Even large quantities can be removed from the blood stream of experimental animals within a few minutes' time. However, it is possible to introduce sodium citrate, especially if in concentrated solution, with sufficient rapidity to exceed the capacity of the oxidation mechanism. The recipients calcium (ionic fraction) is progressively changed to the relatively un-ionized calcium citrate and the signs of calcium deficiency and development of the typical citrate reaction occur. Obviously

the reaction can be produced more easily in an individual already hypocalcemic, or having a small total amount of blood calcium in relation to the dose given as in infants (or experimental animals). From these considerations it is apparent that it is not the total dose of citrate or even the speed of administration alone which must be considered, but the amount of citrate per unit of body weight per unit of time.

The rarity of citrate reactions in our clinical experience indicates that concentrated plasma administered in 15 or 30 gram unit doses (50 to 100 c.c. volume) to adults in from 2 to 5 minutes' time is a safe procedure. We have observed only 8 citrate reactions occurring in 4 patients. Five of the 8 reactions were observed in 2 of the cases. Three reactions were purposely induced to observe the effects and test antidotes. Three cases were children while the fourth was an emaciated white female age 18, who had a marked hypoproteinemia and hypocalcemia associated with steatorrhea. The citrate carpopedal spasm responds dramatically to intravenous calcium chloride or gluconate solution. The reaction may be prevented or stopped at will by 3 to 10 cubic centimeters of these solutions as demonstrated in 2 of the cases just cited. The reaction may also be prevented in these susceptible patients by slow administration of the concentrated plasma, thus allowing sufficient time for the removal of the citrate complex by oxidation. With concentrated serum, of course, these reactions do not occur, and therefore, we prefer this type of concentrated protein solution especially for infants.

In simple hypoproteinemias we have not observed citrate tetany reactions even though total calcium is low in such cases according to McLean and Hastings. This seems to indicate that the ionic fraction alone is involved.

In experimental animals, the citrate reaction is most important in connection with the evaluation of the use of concentrated plasma as we have previously reported (2). When the human size syringe (50 to 100 c.c.) is used on the relatively small animal (dog) it is very easy to give doses of plasma (and citrate) which are huge in relation to the total ionic calcium in the blood stream. For example, 100 cubic centimeters of concentrated plasma given (in a short period of time) to a 10 kilogram dog in 2 to 5 minutes is comparable to 800 cubic centimeters of concentrated or 3,200 cubic centimeters of normal plasma administered to an 80 kilogram human in the same time interval. Obviously such doses are scarcely comparable to those ordinarily given to humans clinically. Ivy and his co-workers have recently stressed the importance of citrate as a deleterious factor, based on extensive experiments in dogs. The dosage per unit of time was large and not comparable to the unit dose of concentrated plasma which we have used for humans. It is unfortunate that this important factor has apparently not been considered by workers who have obtained poor results with concentrated plasma in experimental animals.

In conclusion, citrate reactions are extremely infrequent in adults, are only possible when the quantity given per unit weight of recipient per unit of time is very large. Hypocalcemia of course greatly reduces the amount which may be given by the above standards. This type of reaction in our opinion does not constitute an objection to the use in adults of concentrated plasma or any other type of blood, or blood derivative preparation containing citrate.

Overloading the circulation (sudden hypervolemia). Overloading reactions may occur as the result of failure to observe the contraindications to the use of concentrated plasma but should not be blamed on the product since one of its chief therapeutic actions is to increase blood volume rapidly. In the presence of myocardial damage or cardiac embarrassment concentrated plasma or serum should not be given or, when given, the greatest precautions should be exercised. The prominent conditions in this category include impending or actual heart failure such as in coronary occlusion, constrictive pericarditis, valvular lesions and tumor masses constricting the great vessels.

It must be remembered that concentrated plasma unlike normal or dilute plasma causes a blood volume increase greater than the injected volume. With dilute plasma the volume increase by contrast is less than that

given due to loss of the saline fraction either into the tissues or through the kidney. In the case of concentrated plasma the amount of fluid withdrawn from the tissues depends on the concentration, and the final sustained volume increment depends on the total protein content. The shift of fluids and the volume increase occurs rapidly, within a few minutes' time.

In shock or hemorrhage, in the presence of oligemia, this sudden and sustained increase in blood volume is highly desirable, and there is no danger of overloading the circulation from increased volume. When a definite hypoproteinemia is present there are indications that a contraction (49) of the plasma volume exists. Again there seems little chance of increasing the volume too rapidly.

When overloading occurs, pulmonary edema may develop if the left ventricle is under greater strain than the right, but when the right fails congestive failure may ensue or be aggravated. The immediate treatment is withdrawal of blood from the patient. In cases of massive pulmonary edema concentrated plasma has been of benefit when a preliminary bleeding greater than the expected volume increment has been performed. The procedure seems justified only in cases not responding to the usual medical treatment.

Fibrin embolism. Mayner and Strumia and McGraw (51) have reported fibrin embolism following infusion of normal plasma. This type of reaction is due to factors related to preparation and administration. Due to loss of carbon dioxide during desiccation, dry plasma gives an excessively alkaline solution when redissolved in distilled water, with a resultant hydrogen-ion concentration from 8.5 to 9.0. Protein (fibrinogen?) is precipitated at these levels with formation of fibrin like strands and gelatinous spheres.

Jones and co-workers apparently were the first to realize the importance of the adjustment of the hydrogen-ion concentration of plasma after desiccation. This adjustment was accomplished by filling the bottle containing dry plasma with carbon dioxide gas at atmospheric pressure. When water is introduced, the carbon dioxide is rapidly taken up by the alkaline plasma solution yielding a solution with a hydrogen-ion concentration near normal levels (pH 7.6 to 7.8). Strumia (50) has accomplished the same result by dissolving the plasma in dilute citric acid solution.

We have found both methods to be satisfactory, although the use of carbon dioxide seems more physiological. With the standard vacuum bottle capping device commonly used, the carbon dioxide gas can easily be introduced after the air has been exhausted from the bottle by vacuum pump. The bottle of plasma is then further sealed within an atmosphere of carbon dioxide in a standard tin can. For small scale methods, citric acid may be preferred. We have used 0.35 per cent solution of citric acid to produce concentrated plasma (15 to 20 grams in 45 to 55 c.c.).

We have not encountered any reactions on our service which could be attributed to fibrin embolism, although it seems entirely possible that some fibrin may have been administered. Early in the development of our methods, the fibrinogen content of the plasma was greatly reduced by treatment with filter-cel[1] and Seitz filtration. Later this step was omitted, but a stainless metal filter was designed to be placed into the under surface of the rubber stopper of the plasma bottle to remove such fibrin. At present both the filter and adjustment of the hydrogen-ion concentration of the final plasma solution are used as safeguards.

Hemolytic reactions. Recent papers have indicated the possibility that intravenous plasma therapy is attended by some danger due to a content of isoagglutinins or type specific substances A or B (25, 26, 40), incompatible to the recipient. Polayes and Squillace reported the case of a patient whom they considered to have had a hemolytic reaction following the administration of a bottle of commercial type of dried plasma. The plasma given in normal concentration had an agglutinin titer of 1:16 and was prepared by the usual method of pooling several plasma samples. Mahoney and associates have pointed out the danger of transfusion given in close association with administration of such agglutinin containing plasma. The giving of exceptionally large doses of plasma and the use of

[1] Diatomaceous earth filter aid.

plasma in concentrated form would seem to increase this danger when plasma prepared in the ordinary manner, without complete agglutinin removal, is used.

Levine and State (25, 26) used skin reactions to test whether a given plasma preparation is toxic for an individual. They suggested that reactions might be due to injected type specific substances in the plasma with which the recipient is incompatible.

In defending the use of plasma prepared by the technique of pooling plasma samples, Thalhimer points to the safety of pooled plasma as demonstrated by the small number of reactions seen in world wide use. In his opinion plasmas with agglutinin titers of 1:512 or less can be safely administered regardless of recipients' type and gives evidence to show that pooled plasma may frequently exhibit titers up to 1:30, but not higher than 1:60.

One must certainly agree with Thalhimer that the safety of pooled plasma when given in normal concentration and not combined with whole blood has been amply demonstrated. Nevertheless, further improvement in the safety of plasma preparations is desirable. It would seem that complete or near complete neutralization and removal of the controversial isohemagglutinins by pooling different types of blood would be the logical solution. In this connection one interesting factor has been overlooked. According to Schiff and associates the type specific substances A and B (agglutinogens) may or may not be present in an individual's plasma, and on this basis individuals are classed as secretors and nonsecretors. A nonsecretor having no dissolved agglutinogen in his plasma would be lacking one of the three mechanisms designated by Thalhimer for the neutralization of injected incompatible isoagglutinins. His blood cells and fixed tissue cells would be required to effect all of the neutralization. This would mean more isoagglutinin available for adsorption and action on red cells. It would seem important to investigate whether such individuals have a lower tolerance for incompatible agglutinins. Another consequence of the concept of Schiff would be that plasma from nonsecretors would not be useful in reduction of isoagglutinin titer during pooling since it lacks the type specific A and B substances responsible for partial neutralization or so called suppression of agglutinins occurring in plasma pools. If all plasma units in a pool should chance to be agglutinogen free (i.e. from nonsecretors) no reduction of agglutinin titer except through dilution effects would be expected.

Since any reasonably sized plasma or blood pool will contain relatively large quantities of all isohemagglutinins, it seems difficult to believe that dissolved agglutinogen (A and B substance) can escape neutralization in any quantity, to act as Levine and State claim to cause reactions.

Because isohemagglutinins in plasma can be harmful in high titers and some doubt exists concerning their possible effects in the range usually encountered in pooled plasma, we have come to believe that a safer plasma results when neutralization is accomplished by pooling blood rather than pooling plasma. The agglutinins can be completely neutralized and removed[1] by pooling the various types (A, AB, B, O) of blood in the same reservoir. After pooling, separation is most efficiently and rapidly effected by De Laval separators (13, 15, 16). When such agglutinin-free plasma is used, hemolytic reactions cannot occur. This neutralization, it seems, would also eliminate reactions of the type described by Levine and State and considered by them to be due to type specific substances. All of our plasma has been produced by the blood pooling technique during the last 3 years. When blood that has been stored not longer than 48 hours is used and a low temperature is maintained during pooling, a plasma having a low hemoglobin content (25 to 50 mgm. per cent) can be obtained.

We have frequently given agglutinin-free concentrated plasma prepared by our methods, in conjunction with whole blood transfusions of various types without ill effects. Furthermore, no reactions of the hemolytic type have been observed since the beginning of our dried plasma service in 1939. In evaluating the use of concentrated plasma in respect to its safety it would seem absolutely essential

[1]This removal or neutralization of agglutinins is demonstrated by negative agglutination against A and B cells at 1:1 dilution.

to consider whether agglutinins had been completely or only partially neutralized in its preparation.

MISCELLANEOUS CONSIDERATIONS

Hemoglobin. As previously stated, we have found no evidence that hemoglobin or methemoglobin in plasma causes reactions. We have given 15 to 32 grams of free hemoglobin in saline solution to 8 patients without alarming reactions. Others (1, 5, 12) have found that hemoglobin solutions containing far more hemoglobin than ever encountered in plasma preparations could be administered intravenously with impunity. Yomakami, however, produced fever in rabbits by induced intravascular hemolysis. This method, of course, introduces other factors.

Dehydration. Near critical dehydration entailing very large losses of water from the body (8,000 to 10,000 c.c. in an 80 kgm. person) is an infrequent occurrence found under special conditions of gastrointestinal fistulas, cholera, possibly in water deprivation during desert warfare, etc. Such losses may contraindicate the use of concentrated plasma or more properly stated indicate the urgent need of rehydration with water and salt. Concentrated plasma solutions are not dehydrating in the ordinary sense, since water is not lost by diuresis as in the case of hypertonic glucose but merely shifted from tissues to blood stream. Of course, in the overhydrated person with edema this shift of excessive tissue fluid does result in diuresis.

We have not observed any reactions to concentrated plasma which could be attributed to dehydration, and clinically we have observed to our own satisfaction that in most circumstances under which traumatic shock, burns, and hemorrhage occur there is sufficient fluid in the interstitial and intracellular compartments to dilute large doses of concentrated plasma or serum. If loss of skin turgor is not prominent, concentrated plasma can be given with confidence that adequate amounts of fluid are available for hemodilution without harm to the patient and in the case of shock with benefit to the circulation.

In order to investigate further dehydration in relation to concentrated plasma or serum therapy, such plasma was administered to dogs in the state of near critical dehydration (loss of 7 per cent body weight) induced by glucose diuresis (33). These animals showed a shock-like state with decreased blood volume, hypotension, hemoconcentration, concentration of plasma proteins, weakness, and stupor. Concentrated serum by vein resulted in transient but definite benefit with permanent recovery if followed by water by mouth within 2 hours. Studies of blood volume, fluid distribution, and proteins showed that concentrated serum in dogs is capable of withdrawing fluid from the tissues into the blood stream without adverse reaction even when dehydration approaches the near critical level.

Contamination reaction. Earlier Strumia and McGraw (52) reported a few febrile reactions following normal plasma injections which were attributed to actual contamination by organisms. Rigid techniques and extensive bacteriological controls eliminated these reactions. This possibility is always present when liquid plasma preparations are stored for any length of time. No reactions of this type have been observed in this plasma service since we have stored plasma only in the dry or frozen state both of which conditions prevent bacterial proliferation.

Minor problems. Patients have occasionally complained of a slight dull ache along the course of the vein when concentrated plasma is administered rapidly. By slowing the rate of injection this pain can be stopped. Since the hydrogen-ion concentration of the concentrated plasma has been adjusted as suggested by Jones and co-workers this ache over the vein receiving plasma has been eliminated. This fact is of considerable importance when concentrated plasma is injected intrasternally.

When concentrated plasma or serum is given into the subcutaneous or dermal tissues, it is quite painful for a short time. The pain soon passes and we have never observed a slough from this minor mishap.

In parturient women the administration of the concentrate has on occasions precipitated a low backache which lasts 2 to 8 minutes. This pain seems to be associated with uterine contraction.

In severe shock cases we have on occasions observed a transient hyperpnea following the rapid injection of the concentrate. The hyperpnea lasts 3 to 8 minutes and entails an increase in the respiratory rate; such as from 18 to 24 respirations per minute. The phenomenon seems to be confined to patients with a lowered blood pressure and to those frequently semiconscious and has not appeared to be harmful. We do not know the cause of this occasional transient hyperpnea, but it can be eliminated by slowing the rate of injection or by brief pauses during administration.

The rapid injection of concentrated plasma to patients having an oligemia has not been conducive to what has been termed "speed shock" (20, 22). We have on numerous occasions administered 50 to 100 cubic centimeters of the concentrate in 2 to 5 minutes' time with no observable ill-effects. The condition termed "bulk reaction" (20, 22) seems similar to that discussed under the heading, "Overloading of the Circulation."

Newhouser and Kendrick have described a drop in blood pressure following the administration of concentrated plasma in cases in shock. In several cases we have considered this change due to insufficient therapy in the inception of a blood pressure drop due to shock. In such patients additional therapy in adequate measure has always reversed this change. In dogs in deep shock a transient mean arterial pressure drop has been observed following 5 to 15 cubic centimeters of the concentrate given rapidly (5 to 10 seconds). The drop is usually of 5 to 20 millimeters and lasts 0.5 to 1 minute. After this drop the pressure is elevated to a level above the preinjection level. We have never observed this type of pressure drop in human patients, possibly due to the fact that it would be difficult if not impossible to administer concentrated plasma at a comparable rate with standard syringes and needles. For example, it would be necessary to inject 600 to 800 cubic centimeters of concentrated plasma within 1 minute to the average adult to attain a rate of administration comparable to the experiment here mentioned. This transient depressor effect has been studied and will be discussed in a separate report (36).

We have been unable to differentiate between concentrated plasma and concentrated serum from the standpoint of frequency of reaction production. All but one of the pyrogenic and urticarial reactions reported in Table I resulted from the use of plasma. Our experience with concentrated serum is relatively small, but we have administered both serum obtained by syneresis and that obtained by blood defibrination. In the latter procedure the fibrin is whipped out by a special device (17). In children, there is no doubt that concentrated serum is preferred, because the citrate reactions are not encountered following its use.

It is believed by most workers that fresh serum, obtained by syneresis, is conducive to reactions, but serum over 2 to 3 weeks old is not. We are not in a position to discuss this point, but we can state that fresh serum obtained by defibrination, dried by the adtevac process, dissolved in distilled water and given in concentrated form has not produced reactions in our hands. When Seitz filtration is employed in the preparation of plasma, a partially defibrinated product is obtained which likewise has not been conducive to reactions.

CONCLUSIONS

1. Different types of reactions with particular reference to concentrated plasma are discussed.

2. Reactions are classified according to causative factors; namely factors inherent in plasma or serum, factors introduced during the preparation, factors associated with faulty administration, including contraindications, and peculiarities or idiosyncrasies of the recipient.

3. Properly prepared concentrated plasma is safer than whole blood transfusions.

4. Although plasma prepared by pooling after separation of erythrocytes carries very little risk, greater safety can be obtained by pooling of blood of all different types prior to separation.

5. The reaction rate of plasma prepared in this center is presented. Preparation consists of (a) low temperature pooling of whole blood; (b) separation with two stage continuous

separators; (c) vacuum desiccation from the frozen state; (d) adjustment of the hydrogen-ion concentration of final plasma solution to normal levels, and (e) pyrogen-free water and equipment for administration.

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IMPLANTATION OF THE HEPATIC DUCT INTO THE DUODENUM OR STOMACH

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ANASTOMOSIS between the hepatic duct and the duodenum or stomach may become necessary as a result of operative injury to the common bile duct in the treatment of gall stones or following resection of the common bile duct for carcinoma. Many different methods for securing such an anastomosis have been devised and described, but a review of this literature does not come within the scope of this paper. Many of the methods are unsatisfactory because of technical difficulties or subsequent stenosis. The procedure adopted in the two cases to be described appears to present certain advantages in these respects over those in common use and, since the principle of the method has not, to the authors' knowledge, been heretofore described, this report seems warranted.

CASE 1. Unit No. 221005. A female, aged 35 years, was first seen by us on September 20, 1940. Details of the history and findings are omitted except for certain relevant items. She had been operated upon elsewhere in January, 1940, by a competent surgeon and a cholecystectomy had been performed. The operation was stated to have been accomplished without unusual incident. Symptoms suggestive of biliary colic had been present for the previous 19 years. These were entirely relieved by the operation and the patient states that she felt well for a period of 6 months when she first noticed jaundice and generalized pruritus. Vitamin K and bile salts were administered, but the jaundice steadily increased during the next 2 months and severe colic-like pain appeared in the right upper quadrant of the abdomen on September 18. When seen by us the patient was very deeply jaundiced, the icteric index was 185, and there was no bile in the stools. The prothrombin time was normal, doubtless due to the continued ingestion of bile salts and vitamin K. A diagnosis of obstructive jaundice was made and operation was performed on September 27, 1940. The gall bladder, common bile duct, and free portion of the hepatic duct were all missing. Dense scar tissue on the under surface of the liver was dissected free, and the greatly dilated intrahepatic portion of the bile duct was finally opened. This yielded about 20 cubic centimeters of a colorless mucinous fluid. Since the opening was flush with the liver surface and the region relatively inaccessible, the problem of making a satisfactory anastomosis with the gastrointestinal tract appeared at first quite formidable. Recourse was made to a method that one of us (L. R. D.) had previously used with success in experimental work on dogs. A rubber catheter (No. 18, French), the largest that could be introduced, was inserted snugly into the hepatic duct and passed upward into the liver for a distance of about 5 centimeters. The duodenum had been freely mobilized in the previous dissection in searching for the common bile duct. The catheter was then placed against the anterior wall of the second portion of the duodenum, as illustrated in Figure 1, a, the duodenum was infolded over the catheter for a distance of 2 centimeters with silk sutures in a manner similar to that employed in the Witzel enterostomy. The free end of the catheter was introduced into the lumen of the duodenum and then out again by means of a stab wound 4 centimeters distally as indicated in Figure 1, b. Both the entrance of the catheter into the duodenum and its exit were tightly closed, the latter being reinforced by a generous tag of omentum. Two stay sutures were then placed in the scar tissue, one on either side of the aperture into the hepatic duct. The duodenum was slid along the catheter against the hilum of the liver and held in place by the stay sutures, as illustrated in Figure 1, c. The catheter was thus completely covered. The abdomen was closed in the usual manner and the catheter brought out through the incision. The drainage from the tube remained straw colored for several hours, then became definitely bile tinged and progressively darker until normal appearing bile drained freely. Convalescence was satisfactory except for a moderately severe wound infection. The catheter was removed in 10 days, bile immediately appeared in the stools, but the icteric index remained abnormally high for 3½ months. Jaundice then disappeared and the patient has remained well to date (December, 1942) or over 2 years.

In view of the operative findings the long period (6 months) of good health and freedom from jaundice after the cholecystectomy is

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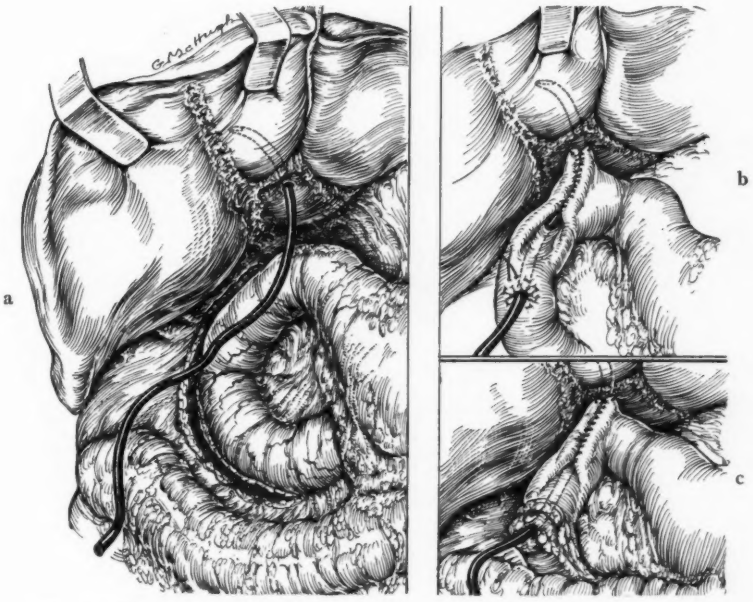

Fig. 1. Illustrating a method for making an anastomosis between the intrahepatic bile duct and the duodenum.

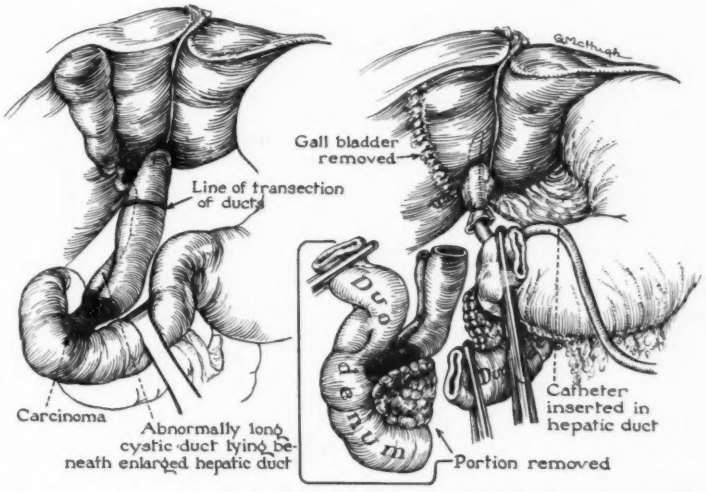

Fig. 2. Drawing illustrating carcinoma of the common bile duct and cystic duct which emptied abnormally low into the common duct.

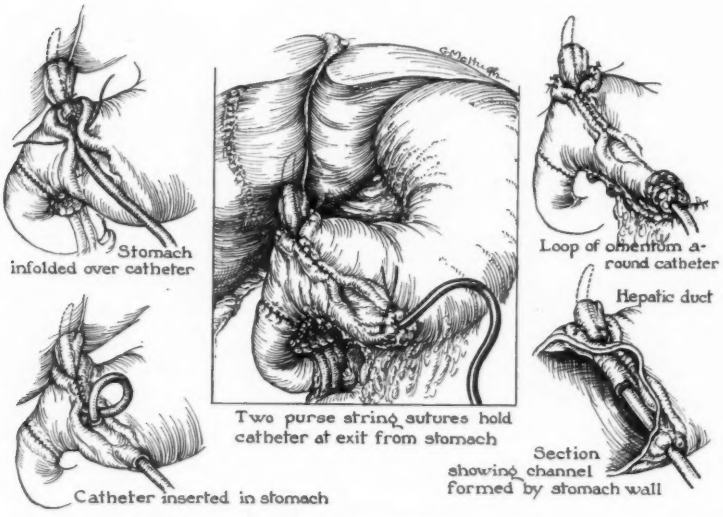
Stomach infolded over catheter
Two purse string sutures hold catheter at exit from stomach
Loop of omentum around catheter
Hepatic duct
Catheter inserted in stomach
Section showing channel formed by stomach wall

Fig. 3. Drawing illustrating method of reconstruction after pancreatoduodenectomy and for implantation of the short hepatic duct into the stomach.

interesting. It seems probable that the ducts were not directly damaged at this operation but that some other factor, possibly interference with the blood supply to the ducts, was responsible for their subsequent gradual disappearance with the onset of obstructive jaundice. The method of repair here illustrated is technically the easiest of those with which we are familiar and the free external drainage of bile is reassuring from the standpoint of liver function in the immediate postoperative period.

CASE 2. Unit No. 270766. Male, aged 67 years, entered the A. M. Billings Hospital November 2, 1941. The details of the history and findings are omitted except for certain relevant items. There was a story of progressive painless jaundice and weight loss of 50 pounds during the previous 10 months. The liver was markedly enlarged, the stools were clay colored, the icteric index was 60, the prothrombin was 86 per cent of normal, and a moderate anemia was present. A diagnosis of obstructive jaundice, probably due to cancer of the head of the pancreas, was made and operation was performed on November 26, 1941. The liver was markedly enlarged, dark green in color, firm, and nodular. The gall bladder was collapsed and contained a small amount of thick gray fluid. The common and hepatic ducts were enlarged and tensely distended to a point where the duct entered the pancreas. The tissues here were hard and fibrous and a tentative diagnosis (subsequently confirmed) of cancer of the common bile duct was made. Pancreatoduodenectomy was performed and the hepatic duct implanted into the stomach as illustrated in Figures 2 and 3. Recovery was satisfactory, bile drained freely from the tube in the hepatic duct until it was removed 2 weeks later. A duodenal fistula then developed and persisted. The subsequent course was characterized by progressive nutritive impairment, weight loss, and cachexia, in spite of almost daily transfusions of blood, plasma, or amino acids. Death occurred March 29, 1942, or 4 months from the operation. Autopsy revealed extreme emaciation, complete absence of subcutaneous and depot fat, and biliary cirrhosis, but without fatty infiltration in the liver. The pancreatic duct was completely occluded, dilated, and the remaining pancreas atrophied and fibrotic. This atrophy was limited to the acinar tissue; the islets were normal.

The absence of fatty infiltration of the liver in this case is significant in view of the complete occlusion of the pancreatic ducts. No pancreatic juice could enter the intestinal tract. This finding is in harmony with our results in the dog following ligation of the pancreatic ducts, and suggests that lipocaic deficiency is not a prominent feature at least in the immediate postoperative period. The emaciation can be accounted for on the basis of the duodenal fistula, the absence of pancreatic digestion, and the impairment of liver

function which doubtless interfered with the utilization of the plasma and amino acids supplied. The plasma protein concentration persisted at a low level and did not respond to parenteral amino acid therapy. The case is presented as offering a satisfactory method of dealing with the hepatic duct after pancreatoduodenectomy, but raises the question—should not the pancreatic duct be reimplanted into the intestine in this operation? Many of these patients with long standing biliary obstruction are handicapped by serious impairment of liver function and for this reason may not respond satisfactorily to the intravenous administration of plasma or amino acids. The complete removal of pancreatic digestion by ligation of the pancreatic ducts produces an additional handicap to adequate nutrition which in some cases may determine the issue. The severed pancreatic duct in the dog may be readily implanted into the small intestine by the method described here for the hepatic duct. In this case, however, infolding is omitted. A small ureteral catheter is tied into the pancreatic duct, made to traverse the small intestine by means of small stab wounds and then led to the exterior. After 4 or 5 days the catheter is removed and the high secretory pressure of the pancreas maintains the new opening into the intestine. It is possible that in some cases this method might also succeed in man. The duodenal fistula doubtless resulted from the anastomosis of the stomach with the horizontal portion of the duodenum, which is partly deficient in peritoneal covering. It would have been better surgical judgment to have closed the duodenum and made an anastomosis with the side of the jejunum.

HEXESTROL

A Comparative Study of Estrogens and Methods of Administration

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THIS report culminates 7 years of experience gleaned from the treatment of some 358 patients with almost all of the estrogenic preparations that have been made available during the past 10 years. A critical review of these 358 cases yields some rather pertinent data as to which of the hormones has been the most effective in our hands, and some very impressive evidence as to which method of administration is productive of the most satisfactory results. In this series of patients we have used from time to time the estrones, the estradiols, emmenin, and more recently the synthetic estrogens, stilbestrol and hexestrol. Before the advent of the synthetic hormones, our policy had been to attempt to time the administration of the estrogens in such a way as to imitate the normal, cyclic production of this hormone by the human ovary. This method of administration we have chosen to term "estrogenic therapy in phase" as opposed to "continuous mass dosage," wherein relatively large doses are given at regular specified intervals without regard to the physiologic hormone cycle with which nature seems to do so well. While we have accumulated impressive statistics on the "in phase" administration of the so called "natural estrogens" in relatively small doses, unfortunately we have no data on such a method of administration of hexestrol, and diethylstilbestrol was given in this manner in so few cases that the results are not significant.

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Dr. Schloss, now Lieutenant, M.C., U.S.N. on active duty.

Dr. Lyford, a young, skillful, exceptionally well trained gynecologist and a founder of the Gyn-Dysfunction Clinic of the Cincinnati General Hospital, died February 15, 1943, after a short illness. He was an ardent advocate of the "in phase" method of administration and the figures here compiled attest to the soundness of his teaching. J. G. C.

The pharmacologic and physiologic activity of the "natural estrogens" estrone, estradiol, and emmenin have been so thoroughly discussed in the past, that we shall merely tabulate our experience with these hormones administered "in phase."

TABLE I.—IN PHASE ADMINISTRATION

	Cases	Per cent	Mean treatment time months
Symptom free	62	45.25	5
Improved	51	36.50	4.6
Unimproved	24	18.25	4.25
Mean treatment time for group			4.7

The development of the stilbestrol series of estrogenic substances began with the demonstration by Dodds and Lawson in 1937 that anol (p-hydroxypropenyl) undergoes polymerization and yields traces of a highly active estrogenic substance, one of the most potent of which is dihydroxy-alpha-beta-diethyl stilbene, or diethylstilbestrol. In clinical use, however, the administration of diethylstilbestrol was attended by toxic reactions exhibited chiefly as nausea and vomiting.

Further intensive research was carried on for other active polymers of anol in the hope of finding a compound with high estrogenic activity and comparatively low toxicity. Campbell, Dodds, and Lawson (3) isolated from anol a highly active polymer, 4:4′ dihydroxy-gamma; delta-diphenyl-n-hexane which was identical with the hydrogenated form of diethylstilbestrol, dihydroxy-diethylstilbestrol. These authors found that this latter substance, which was called "hexestrol," in doses of 0.15 microgram gave an estrus response in 60 per cent of rats, whereas a dose of 0.1 microgram gave a 20 per cent response. A dosage of 0.2 microgram caused full estrus in all rats. It appeared that, in the rat, hexestrol was more active than diethylstilbestrol in producing vaginal estrus.

Campbell and coworkers (4) further tested the biological activity in ovarectomized rabbits, male guinea pigs, and ovarectomized rats. Comparative activity of diethylstilbestrol, hexestrol, and estradiol was determined in the 60 rats, and it was found that hexestrol was most active, being slightly more active than diethylstilbestrol and 2.8 times more active than estradiol.

The first reported clinical study of hexestrol was made by Bishop and his associates. Their chief object was to determine threshold doses of diethylstilbestrol, diethylstilbestrol dipropionate, and hexestrol rather than to obtain a high percentage of satisfactory clinical results. Of 103 menopausal patients 63 were treated with hexestrol, 60 with diethylstilbestrol dipropionate. Relief was obtained in 91.2 per cent. Comparative clinical activity could not be established by this regimen, but the toxicity incidence, studied in 155 cases, was 21.6 per cent for diethylstilbestrol and the dipropionate, and 4.5 per cent for hexestrol. (In a private report appended to this publication, Bishop reports toxicity studies in a series of 83 patients treated with diethylstilbestrol, 20 with diethylstilbestrol dipropionate and 18 with hexestrol. Toxic symptoms developed in 22.9 per cent with diethylstilbestrol, 30 per cent with diethylstilbestrol dipropionate, and in none with hexestrol. The maximum daily dose of hexestrol in this series was 2 milligrams orally.)

The comparative estrogenic activity of hexestrol and diethylstilbestrol in the human has been studied by Freed who found that 3 to 5 milligram doses of hexestrol were necessary for satisfactory relief in a group of menopausal patients who had been controlled with 0.5 to 1 milligram of diethylstilbestrol. Thus the activity in the human of hexestrol was, according to this report, one-fifth that of diethylstilbestrol. Incidence of toxic reactions with hexestrol was about one-half that with diethylstilbestrol, the incidence in the latter being 15 per cent. Toxic reactions with hexestrol (nausea and vomiting) were mild and seldom necessitated withdrawal of the drug.

Bieren and Compton found in small series of patients with menopause, primary dysmenorrhea, and senile vaginitis that the activity of hexestrol was only one-tenth that of diethylstilbestrol. On the other hand they found that in treating vulvovaginitis of children hexestrol was slightly more effective than equal doses of diethylstilbestrol. Some patients responded to large doses of hexestrol that had not responded to small doses of stilbestrol. Nausea was experienced in some, but it was of mild nature.

The discrepancy in estrogenic activity of hexestrol in the two latter reports indicate that much more study in larger series of patients is necessary before any definite statement as to the comparative activity of hexestrol and diethylstilbestrol can be made.

Aside from the results here discussed, little or no data are available regarding the pharmacology and toxicology of hexestrol. Preliminary results (8) of a recent investigation indicate the close similarity between the activity of hexestrol and stilbestrol. Assayed subcutaneously in olive oil by the method of Kahnt and Doisy 0.35 gamma of hexestrol was found equivalent to 0.4 gamma of either stilbestrol or alphaestradiol benzoate. These results compare favorably with those obtained by Campbell and associates (4). Hexestrol and stilbestrol administered in large doses every other day for a period of 3 months inhibited the rate of growth and weight increase in ovarectomized females, normal females, and male rats. The toxic changes observed were similar to those described by Teague. The adrenals were enlarged and dark brown in appearance, the hypophyses of many of the animals were hypertrophied, the gonads of both the male and female animals were atrophied, and the uterus and vagina resembled those of estrous animals. Pyometria occurred in some of the rats. Hexestrol and stilbestrol produce a like increase in the weight of the uteri of immature mice indicating a similarity in action. This action was also observed by Campbell (4).

On the basis of the available animal experiments it would, therefore, appear that the toxicity and estrogenic activity of stilbestrol and hexestrol are very similar.

One of the pitfalls in the evaluation of response to estrogenic therapy has always been the close similarity of the symptomatology of the menopausal syndrome and that of neuro-

circulatory asthenia and the various psychoneurotic states. Several clinics have from time to time substituted sterile oil or saline for the injectable estrogens and have noted relief from symptoms, comparable in many instances with the results obtained with estrones and estradiols. Another of the variables encountered is the very obvious fact that our private patients respond much more quickly and completely to estrogenic therapy than do their sisters in the free clinics and dispensaries. Several reasons have been given for this, the most universal being the economic reality that the private patient, having to pay for her treatment, strives for release from medical expense as well as from her symptoms, and this in turn acts as a very definite psychic boost along the road to recovery. The return of good times and increased employment incident to war work has also been a great psychic aid to symptomatic relief. Patients who have responded indifferently in the past, quickly recover so that they can get easily available and remunerative work at nearby defense plants. Women, whose husbands and sons have long been idle and on relief rolls, improve markedly as these unemployed begin to bring home pay checks which insure more and better food, entertainment, and the other desirable things in life. Conversely, some patients who were getting along quite well experienced marked exacerbation of symptoms when sons were drafted into the army, or when military action was reported in areas where sons already in the services were known to be stationed. Unquestionably, favorable or unfavorable psychic influences can alter greatly the response of these patients to our best attempts at effective estrogenic therapy.

Weather is another very definite factor which must be taken into consideration. We have noted much more difficulty in controlling symptoms of menopause during spells of high humidity, and it is undeniable that the patient in the climacteric sleeps better, feels better, and enjoys much more freedom from hot flushes, fatigue, headaches, and vertigo in cool, dry weather than at any other season of the year.

As has been previously noted, diethylstilbestrol was the first of the synthetic estrogens to be produced for clinical use. The consensus has been that this preparation is an effective estrogen, whether given by the oral route, by the application of ointments and suppositories, by the intramuscular injection of oily solutions, or by the implantation of crystals and pellets. It has been of great value in the relief of the untoward symptoms of the female climacteric, but favorable reports have also been forthcoming on its efficacy in the treatment of various other conditions in which a potent estrogen is indicated. Its use in the relief of essential dysmenorrhea has been favorably commented on by Sturgis, and Russ and Collins have found it effective in the treatment of gonorrheal vulvovaginitis and in the senile vaginitis of the postmenopausal years. Muchle has presented conclusive evidence of the value of stilbestrol in the suppression of lactation, and its ability to decrease the insulin requirement of the diabetic in pregnancy has been reported by White and Hunt, and in the menopause by Spiegelman. Many writers, notably Sevringhaus, have reported favorably upon the efficacy of stilbestrol in the menopause. That it may be of value in the treatment of hyperemesis gravidarum seems not unlikely from the work of Smith and Smith, who found that its administration along with progesterone had a definitely beneficial effect on the nausea and vomiting.

For the past 2 years we have been treating all patients with hexestrol by the method of "continuous mass dosage."

For purposes of comparison our experience with continuous mass dosage using all estrogenic hormones except hexestrol is compiled in Table II.

TABLE II.—ADMINISTRATION BY CONTINUOUS MASS DOSAGE

	Cases	Per cent	Mean treatment time—months
Symptom free	17	15.35	8.23
Improved	52	46.85	6.5
Unimproved	42	37.8	7.8
Mean treatment time for the group			7.35

From the figures in Table II it will be seen that administration of all estrogens except hexestrol by continuous mass dosage produced only 15 per cent of symptom free results as

compared with 45 per cent by in phase administration; 38 per cent of complete failures as compared with 18 per cent; and a total satisfactory result (symptom free and improved) of 62 per cent as compared with 79 per cent for the in phase method. The latter also gave results in a significantly lesser treatment time, 7.35 months for continuous mass dosage and only 4.7 for in phase therapy.

Our experience with hexestrol by continuous mass dosage, summarized in Table III, shows a higher incidence of satisfactory results and a lesser incidence of complete failures than either of the previously detailed methods, with a treatment time not appreciably less than that of in phase administration. The latter still is superior as far as completely symptom free results however, with 45 per cent as compared to 28 per cent with hexestrol. It seems logical to suppose that hexestrol, administered by the in phase method, would be far superior to any type of therapy yet tried, and it is our plan to run such a series of cases with this new synthetic estrogen.

TABLE III.—CONTINUOUS MASS DOSAGE (HEXESTROL)

	Cases	Per cent	Mean treatment time—months
Symptom free	31	28.2	5.5
Improved	63	57.3	5.5
Unimproved	16	16.5	5.3
Mean treatment time for group			5.4

In our series of cases on hexestrol, 130 patients have been treated for various gynecological complaints; these cases are distributed as follows: surgical menopause, 55; natural menopause, 55; senile vaginitis, 3; amenorrhea, 1; oligomenorrhea, 2; menometrorrhagia, 2; dysmenorrhea, 12 cases.

The menopausal symptoms encountered with percentage incidence were as follows: hot flushes, 96, 87.3 per cent; insomnia, 57, 52.0 per cent; nervousness, 52, 47.3 per cent; fatigue, 50, 45.4 per cent; headache, 49, 44.5 per cent; emotional lability, 20, 18.2 per cent; arthralgias, 17, 15.5 per cent; vertigo, 17, 15.5 per cent; others, 15, 13.6 per cent.

Results. The total results in all types of cases have already been tabulated (Table III). The results in the individual case groups are shown in Table IV—Results in Individual Case Groups.

TABLE IV.—RESULTS IN CASE GROUPS

Surgical menopause	Cases	Per cent	Mean treatment time—months
Symptom free	13	27.0	7.25
Improved	30	62.5	6.25
Unimproved	5	10.5	5.4
Unsuitable for treatment	3		
Insufficient time for evaluation	4		
Treatment discontinued because of untoward effects (Nausea and vomiting, 2; nausea only, 5)	7		
Mean treatment time for group			6.4
Natural menopause			
Symptom free	8	16.7	3.75
Improved	33	68.7	4.7
Unimproved	7	14.6	5.3
Unsuitable for treatment	1		
Insufficient time for evaluation	6		
Treatment discontinued because of toxic effects (Nausea, 2; chills and urticaria, 1; headache and conjunctivitis, 1)	4		
Mean treatment time for group			4.6

Senile vaginitis. Three patients with senile vaginitis were treated, 2 of them with quite satisfactory results. Only the oral route was used in these cases, but we are of the opinion that the use of hexestrol in the form of vaginal suppositories would have hastened and made more complete the clinical result.

Amenorrhea. Only 1 patient with amenorrhea was treated. While withdrawal bleeding of a very small amount was noted, this patient had previously been subjected to pituitary irradiation for this purpose, and it is impossible to evaluate the result. She has bled cyclically without hexestrol since the irradiation treatment.

Oligomenorrhea. Two patients with scanty menstruation were treated with hexestrol. One has been under observation only 2 months at the present writing and as yet no improvement has been noted. The other had been treated for 8 months with amniotin and 2 months with diethylstilbestrol. After 3 months of 1.0 milligram of hexestrol daily, she bled so profusely that another preparation had to be used to check the bleeding. She did not return to the clinic thereafter.

Functional bleeding. Two patients with functional bleeding were treated. In 1 there was complete failure, and x-radiation was decided upon in preference to further trial with hexestrol. The second patient had apparently satisfactory improvement in one menstrual cycle, but has not been under observation long enough to justify any claims.

Dysmenorrhea. In the treatment of dysmenorrhea, we have had some truly brilliant results, just as we have previously noted with diethylstilbestrol. We have reserved the use of hexestrol for the refractory case which has resisted the more commonly used analgesics and antispasmodics. The cases we have treated have been only the failures of other forms of treatment including dilatation and curettage, uterine suspension, and presacral sympathectomy. Since the theory is that a large dose of estrogen, such as represented by hexestrol, inhibits the pituitary, which in turn fails to bring about follicle maturation and rupture, thus inducing anovulatory bleeding which is painless, we do not believe that it is to be recommended for widespread or continuous use. But for the clinician who wants to secure prompt symptomatic results so as to gain the confidence of his patient, while he studies her case more carefully and at greater length, hexestrol is suggested for cautious administration under careful observation. Of the 12 patients treated, complete symptomatic relief was noted in 9. The 3 others were failures.

Toxic effects. Toxic effects in the incidence listed below were noted in 23 cases; in only 11 cases were these severe enough to necessitate discontinuance of hexestrol: nausea only, 13 cases; vertigo, 4; nausea and vomiting, 2; epigastric pain, 2; headache with conjunctivitis, 1; chills with urticaria, 1; making a total of 23. The 11 necessitating discontinuance were distributed as follows: nausea only, 7 cases; nausea and vomiting, 2; chills and urticaria, 1; headache and conjunctivitis, 1, making a total of 11.

Dosage. The dosage of hexestrol was so variable that it is impossible to tabulate it in any kind of statistical form. Suffice it to say that the incidence of untoward symptoms from the drug bore no relationship to the dosage given. The amount administered has varied from 0.2 milligram every other day up to as high as 3.0 milligrams twice daily for the oral preparation, and 1.0 milligram from one to three times weekly for the intramuscular route. Toward the end of the series our tendency was to start our menopausal cases out on 3.0 milligrams by mouth daily and 1.0 milligram in oil twice weekly by the intramuscular route. This schedule was maintained until some amelioration of symptoms was noted, after which the dose was reduced gradually to the lowest amount compatible with a satisfactory symptomatic result. While in some cases this was accomplished with a dosage as low as 0.2 milligram every other day orally, the usual maintenance dose was 1.0 milligram orally daily. Intramuscular administration was continued at least once a week until we were sure the patient was getting a good symptomatic result, and in a few cases intramuscular medication alone was used as the patients seemed to respond better to this method of management. Whether this was due to the greater efficiency of intramuscular dosage, or to the greater psychic effect of this more impressive procedure must be left for conjecture; probably both factors play a part.

The 11 cases with untoward symptoms necessitating discontinuance of hexestrol are listed below together with the dosage used:

1. Nausea and vomiting: 1.0 mgm. daily orally only.
2. Nausea and vomiting: 1.0 mgm. every other day: subsequently this patient was again placed on hexestrol and tolerated 1.0 mgm. daily with a satisfactory result clinically.
3. Nausea only: 0.2 mgm. twice daily.
4. Nausea only: 1.0 mgm. every other day.
5. Nausea only: 1.0 mgm. daily.
6. Nausea only: 0.2 mgm. daily.
7. Nausea only: 1.0 mgm. weekly, intramuscularly.
8. Nausea only: 1.0 mgm. 2 times weekly, intramuscularly.
9. Nausea only: 1.0 mgm. daily.
10. Chills and urticaria: 1.0 mgm. twice daily orally and 1.0 mgm. 2 times weekly, intramuscularly.
11. Headache and conjunctivitis: 1.0 mgm. 2 times weekly, intramuscularly.

Of these 11 cases in only 1, the patient with chills and urticaria, can the dosage be said to have been large. In all the rest the amount of the drug administered was relatively trivial when compared to the massive doses given to many patients with perfectly satisfactory clinical improvement.

On the other hand, clinical improvement was by no means proportionate to the amount of the drug administered. In some of the most satisfactory clinical results the dosage was as low as 0.2 milligram daily or every other day, while some of the failures received relatively huge amounts of the drug.

In most instances such untoward symptoms as nausea, bleeding, vertigo, and epigastric distress could be controlled by drastically reducing dosage, and then stepping it up again as the toxic effect disappeared. Bleeding was controlled by discontinuing the drug for about 1 week and then resuming it in a more cautious and more carefully observed program. Bleeding in 2 cases was controlled by the administration of small doses of semandren, a male hormone preparation.

One of the most important points in evaluating the usefulness of a new synthetic estrogen is its capacity to function without the untoward effects of the old. As previously pointed out, one of the greatest drawbacks to the use of diethylstilbestrol has been the comparatively high incidence of so called toxic effects, which have been reported in as many as 80 per cent (12) of the cases treated. In our series we have administered hexestrol to 46 patients who had previously been on diethylstilbestrol. The results of this study are tabulated as follows: nontoxic on hexestrol or stilbestrol, 30 cases; toxic on stilbestrol; nontoxic on hexestrol, 10 cases; toxic on hexestrol; nontoxic on stilbestrol, 2; toxic on both hexestrol and stilbestrol, 1; improvement on stilbestrol, not on hexestrol, none; improvement on hexestrol, not on stilbestrol, 3.

SUMMARY AND CONCLUSIONS

1. Our experience of 7 years, with estrogenic therapy in the Gyn-Dysfunction Clinic of the Cincinnati General Hospital is reviewed.

2. A review of the cases of 358 patients treated during this period would indicate that hexestrol is the most effective of the estrogens we have investigated.

3. Continuous mass dosage of hexestrol appears to result in a lesser incidence of complete failures, while "in phase" administration produces the greater percentage of completely symptom free results.

4. Hexestrol causes a much smaller percentage of "toxic" effects than diethylstilbestrol, but must be administered in from three to five times the dosage of the latter drug to secure the same clinical result.

5. From a consideration of all the data accumulated, it would seem that the best clinical results might be expected from the administration of hexestrol "in phase."

NOTE.—The Wm. S. Merrell Company were most helpful in the compilation of these data. They, as well as E. R. Squibb and Company, Ayerst, McKenna and Harrison, The Schering Corporation, Winthrop Chemical Company, and the S. E. Massengill Company, each furnished some of the estrogens used in this study.

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HAZARDS CONNECTED WITH THE TREATMENT OF VARICOSE VEINS

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WITHIN recent years I have been impressed with the number and variety of mishaps which may occur as the direct result of treatment designed to obliterate varicose veins. These are not complications which supervened because of some basic contraindication to the particular form of therapy employed. On the contrary, they must be considered as definite hazards which are indigenous to certain methods or are the result of either improper technique or the failure to observe certain precautions. These untoward incidents do not occur with sufficient frequency to justify the assumption that the management of varicose veins is a hazardous undertaking. However, to the physician who has the misfortune of being responsible for a serious complication resulting from the treatment of such an apparently benign condition as varicose veins, the low incidence of that particular complication affords dubious consolation.

The present day management of the majority of cases of varicose veins is based on the resection of the proximal end of the great saphenous vein and the subsequent injection into the varicosities of a sclerosing solution. The operative procedure is popularly known as a ligation, a particularly unfortunate term. It has been repeatedly demonstrated that a simple tying off of the upper end of the saphenous vein is frequently followed by a recurrence of the varicosities at some subsequent date even though all varices are adequately obliterated at the time. (For a particularly excellent discussion of this phase of the subject the reader is referred to an article by Stalker and Heyerdale.) Properly executed, the operation essentially consists of a division of the great saphenous vein at a point just distal to its entrance into the femoral vein and a resection of its proximal 2 inches. The operator who is not thoroughly acquainted with the numerous variations in the normal and pathological regional anatomy may encounter considerable difficulty.

Although not personally responsible for these two particular accidents, I have had the opportunity of observing cases in which the femoral vein was inadvertently tied or the femoral artery injured. Hemorrhage is not an infrequent occurrence. The saphenous vein and bulb may be enormously dilated and very thin, or, in the presence of a long standing varicose phlebitis or ulceration, these structures may be brittle and friable and surrounded by inflammatory tissue. Under such circumstances, injury to the vein may be difficult to avoid and the resultant bleeding profuse and hard to control.

CASE REPORTS

CASE 1. A 56 year old white female gave the history that for 25 years she had suffered from varicose veins and painful ulcers on her foot and leg. The ulcers would intermittently heal and then recur.

Examination revealed large, tortuous varicosities along the inner portion of the thigh, leg, ankle, and foot. The Trendelenburg test was singly positive and the Perthes test was negative. The medial aspect of the lower half of the leg was scarred and indurated and presented a large chronically inflamed ulcer.

Resection of the saphenous bulb was advised. The operation was performed under local anesthesia. The upper end of the great saphenous vein was exposed and found to be imbedded in dense inflammatory tissue. It was mobilized with difficulty and divided between ligatures. At this point the operation should have been terminated. However, the dissection was carried further, and in an attempt to mobilize a large lateral tributary of the saphenous bulb, the branch was torn. Profuse hemorrhage resulted. A clamp placed on the injured vein only increased the size of the tear. Finally, the only recourse was to pack the wound. The pack was removed in 3 days and bleeding recurred. The wound was again packed. Three days later the pack was again removed without recurrence of bleeding.

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However, at this time the patient exhibited evidence of femoral vein occlusion. The leg became edematous and has remained so. The ulcer has increased in size.

The retrograde injection of a sclerosing solution into the distal portion of the divided saphenous vein at the time of operation is a widely accepted procedure. I am acquainted with 5 instances in which this maneuver was followed by a thrombosis of the deep veins of the thigh. Two of these patients died from pulmonary embolism, 1 suffered a pulmonary embolus but recovered, each of the other 2 developed a "milk leg" with permanent disability. As will be demonstrated later, anything injected into the saphenous system of a leg rapidly enters the deep venous system of that extremity. Ordinarily, thrombosis of the deep venous tree does not follow injections of sclerosing solutions into superficial varicosities because the patient is ambulatory, the deep venous tree is widely dilated, and the current of blood is swift, and hence the solution is rapidly diluted and does not have the opportunity to irritate the intima sufficiently to produce thrombosis. As will be demonstrated, there are even exceptions to this rule. However, when an individual is necessarily recumbent for a few hours during and after an operative procedure, the deep venous tree is not widely dilated nor the current of blood as swift. Consequently, any sclerosing solution finding its way into the deep veins has a better opportunity of irritating the intima sufficiently to produce subsequent thrombosis.

CASE 2. A 45 year old white male was seen at the request of his attending surgeon. Three months previously he had had a high resection of his great saphenous vein with retrograde injection of a sclerosing solution down the distal portion of the vein. Three weeks later he was suddenly seized with severe pain in the leg, thigh, and groin. Shortly thereafter the entire leg became swollen up to the groin. He was in bed for 9 weeks. Since resuming activity the same swelling recurs by the end of the day. Examination revealed an edematous lower extremity. The extent and distribution of the edema were characteristic of an iliofemoral thrombosis. He was advised to wear an elastic stocking, to sleep with his leg elevated, and to receive a mercurial diuretic as often as it could be safely given.

CASE 3. A 70 year old white male was seen at the request of his attending surgeon. Five days previously he had had a high resection of his great saphenous vein with retrograde injection of a sclerosing solution. Within 24 hours the entire length of the varicose saphenous vein became hard, red, and painful. Three days after the operation he was suddenly seized with substernal distress, dyspnea, and a feeling of faintness. At first it was thought that the man had suffered an acute coronary occlusion. However, competent investigation by a consultant established the diagnosis of pulmonary embolism. This patient recovered. This man had a widely dilated and tortuous great saphenous vein which had thrombosed from ankle to groin as the result of a single retrograde injection.

CASE 4. A white male, aged 61 years, entered the peripheral vascular clinic at Cleveland City Hospital complaining of varicose veins of many years' duration. Examination revealed large varices involving the great saphenous system with a singly positive Trendelenburg test and a negative Perthes test. A resection of the upper end of the saphenous vein was performed. At the time of operation 2 cubic centimeters of quinine urethane were injected down the distal portion of the divided saphenous vein. Three weeks later he was suddenly seized with severe dyspnea, cyanosis, dizziness, and weakness. He was admitted to the medical service in a state of shock. He was treated vigorously but did not respond and expired within 48 hours.

Autopsy revealed massive embolism of the pulmonary artery with evidence of several additional pulmonary infarctions of recent origin. The external iliac vein on the side operated upon was thrombosed. The thrombus extended down into the femoral vein. *The thrombosed iliofemoral vein exhibited no evidence of inflammation and the thrombus was not attached to the vein wall.* This latter observation is of great importance. It confirms what I have repeatedly observed in cases of postpartum, postoperative, and posttraumatic thrombosis of the deep veins of the leg, that a thrombus may remain in the iliofemoral vein for weeks without exciting an inflammatory reaction in the vein wall that will fix the clot *in situ* and abolish the danger of pulmonary embolism.

To prevent this leakage of sclerosing solution through the communicating veins in the thigh into the deep venous tree it has been suggested (7) that the injection be made through a ureteral catheter which has been passed down the length of the divided saphenous vein. As will be demonstrated, deposition of sclerosing solution distal to the knee does not safeguard against leakage of the solution into the deep veins of the leg with subsequent thrombosis and pulmonary embolism. Besides, the passage of the catheter may injure the vein wall, the fluid leaks into the perivenous tissue, and a massive slough ensues.

CASE 5. A 47 year old white female who complained of severe pain in the leg presented the following picture: large varices involving the great saphenous system, a singly positive Trendelenburg test, a negative Perthes test, and a tender area of induration surrounding a varix in the medial aspect of the lower third of the leg. A resection of the upper 2 inches of the saphenous vein was performed. A ureteral catheter was passed down the divided saphenous vein. An obstruction to the passage of the catheter was encountered about 15 centimeters from the fossa ovalis, the catheter was withdrawn rotated and passed beyond the obstruction without any apparent further difficulty. Ten cubic centimeters of a hypertonic saline-glucose mixture was injected through the catheter. During the injection she complained of severe pain in the thigh. Unfortunately, the pain was interpreted as being due to venospasm and the injection was completed. The following day there was an area of necrosis 4 inches in diameter at the site where the obstruction to the passage of the catheter had been encountered. During the ensuing month this entire area sloughed down to the deep fascia of the thigh. Healing was slow and the patient was left with an unsightly scar.

The injection of sclerosing solution directly into varicosities in an ambulatory patient may also be followed by unfortunate events, both local and general.

It should be realized that these sclerosing solutions rapidly enter the general circulation where they may, in the sensitive individual, produce alarming and occasionally fatal reactions. The literature is replete with reports of such untoward incidents. Several years ago one of our clinic patients reacted fatally to an injection of quinine urethane. We have also had several alarming reactions to sodium morrhuate. Similar reactions have been reported to follow the injection of monolate (1, 3).

Locally, three complications to the injection of sclerosing solutions are encountered which are of considerable importance. They are ulceration, phlebitis, and thrombosis of the popliteal vein. Ulceration follows the deposition of certain sclerosing solutions outside the vein. Solutions of quinine urethane and hypertonic saline-glucose mixtures are the worst offenders. The accidental perivenous injection of such solutions as sodium morrhuate, monolate, sylnasol, and soricin is less prone to produce a slough but may cause painful areas of induration which require a long time to absorb. The obliteration of varices by the injection of sclerosing solutions depends for its success on the production of a chemical phlebitis. Consequently, some pain is to be expected at the time and for a short while subsequent to the injection of a varix, and patients should be warned that the injection treatment of varicose veins is not a particularly pleasant experience. At times, an individual over-reacts to the injection of a varix with a chemical phlebitis of such severity that he is disabled for days or weeks. By far the most serious complication of the injection treatment of varicose veins is thrombosis of the popliteal vein. This extremely serious complication may follow the injection of a varix anywhere distal to the knee and may occur in the simplest type of case. The following case report is illustrative.

CASE 6. A 42 year old white female was admitted to the varicose vein clinic at Cleveland City Hospital with the complaint of a painful varicose vein in the left leg. Examination revealed a single moderately sized varix located at the medial aspect of the left calf. Both the Trendelenburg and Perthes tests were negative.

One-half cubic centimeter of 5 per cent sodium morrhuate was injected into the varix as a test dose for any sensitivity to the drug. (The injection of a small quantity of sclerosing solution as a preliminary measure is routinely employed in ruling out sensitivity to the drug.) Three days after the injection she visited the clinic complaining of severe pain in the leg and swelling about the ankle. Examination revealed the varix to be completely thrombosed. The attending surgeon advised her to stay in bed with the leg elevated until the pain and swelling had subsided. She remained in bed for 3 days when she was suddenly seized with an attack of substernal pain, tachycardia, and prostration. She was admitted to the medical service where a diagnosis of pulmonary embolism and an acute cor pulmonale was made. A few days later she experienced another similar attack, and I was asked to see the patient to determine the advisability of ligating the femoral vein.

Examination. The popliteal vein could be palpated as a tender thrombosed cord. There was tenderness deep in the calf of the leg, and Homans' sign (4, 5) was positive. The foot was cold to the touch. There was slight edema about the ankle. The following morning, under local anesthesia, the femoral vein was divided between ligatures just distal to the point of entrance of the profunda. The femoral vein contained no thrombus. Following operation, the patient made an uneventful recovery.

I was particularly disturbed by this case for several reasons. This patient presented

the most simple type of case of varicose veins. There was a single varix limited to a small segment of the great saphenous vein in the middle third of the leg. The negative Trendelenburg test indicated that the valves in the great saphenous vein as well as those in the communicating veins were competent. There was no evidence of a pre-existing deep venous obstruction. Finally, only a very small quantity of sclerosing solution had been used; not in an attempt to thrombose the varix but rather for the purpose of determining sensitivity to the drug. Because of this case and because of the large number of reports of pulmonary embolism following injection of varicose veins which have lately appeared in the literature (2, 6, 9) I was led to investigate what happens to solutions that are injected into the normal great saphenous vein. For this purpose young adults with normal peripheral venous systems were used. Thirty cubic centimeters of 35 per cent diodrast were injected into the great saphenous vein in the lower third of the leg and x-ray pictures taken of the entire length of the lower extremity. Figure 1 depicts what was regularly observed. The radio-opaque solution rapidly found its way into the lesser saphenous vein through anastomoses between the lesser saphenous vein and the injected great saphenous vein. This passage into the lesser saphenous took place in the region of the middle third of the leg. Once in the lesser saphenous vein, the diodrast easily and quickly found its way into the popliteal vein since the lesser saphenous vein joins the popliteal vein behind the knee. The superficial femoral vein is simply the proximal extension of the popliteal vein; hence entrance of fluid into the lesser saphenous vein is practically equivalent to a direct injection into the femoral venous system. Figure 1 illustrates that by far the greatest portion of a quantity of solution injected into the distal major saphenous vein leaves the extremity via the femoral venous system.

Fig. 1. Venogram depicting direction of flow of a radio-opaque solution when injected into a normal great saphenous vein in the lower third of the leg. *N*, Infusion needle in great saphenous vein; *L.S.V.*, lesser saphenous vein; *P.V.*, popliteal vein; *S.F.V.*, superficial femoral vein; *F.V.*, femoral vein; *G.S.V.*, great saphenous vein just distal to point where it passes through fossa ovalis to join femoral vein. Note anastomoses between great and lesser saphenous veins in middle third of leg and that bulk of fluid passes through the lesser saphenous, popliteal, and femoral veins.

CONCLUSIONS AND PRECAUTIONS

The obvious inference to be drawn from the preceding discussion is that the modern method of managing varicose veins contains certain inherent risks that can lead to more or less serious complications. Fortunately, by the observation of certain precautions, these accidents can be avoided.

Resection of the upper end of the great saphenous vein, commonly termed high ligation, is definitely not an office procedure. The operation should be performed in an adequately equipped surgery with assistance so that proper exposure of the bulb and all its tributaries is feasible and so that any emergency such as hemorrhage can be managed.

Although many will disagree with me on this point, I believe that the retrograde injection of a sclerosing solution at the time of division of the great saphenous vein is hazardous and should be avoided. I would much rather subject the patient to extra injections after he has recovered from operation and become ambulatory than expose him to the dangers of a possible iliofemoral thrombosis.

Sensitivity to the sclerosing solution used should be determined by a very small preliminary intravenous injection of the drug, preferably into the varix to be subsequently thrombosed. A history of hives, asthma, hay fever, and particularly reactions to eating fish indicates the use of hypertonic saline-glucose as the sclerosing agent. When this solution is used the patient should be warned that a severe cramp in the leg will accompany or immediately follow the injection. Quinine urethane is a dangerous solution and its use should be discontinued. Care should be taken to avoid injecting any sclerosing solution outside the vein. I prefer to inject varices with the patient standing. The varix is fully dilated and difficulty in entering is rarely met.

Prevention of leakage of sclerosing solution into the popliteal vein through the lesser saphenous vein is of paramount importance. Before a varix either in the thigh or leg is injected, a tourniquet is placed so that it fits into the crease behind the knee. At this point the lesser saphenous vein can be occluded just before it dips into the popliteal space to enter the popliteal vein. The tourniquet is left *in situ* for 5 minutes after the injection has been given. The patient stands during the entire procedure, and after the tourniquet is removed he is instructed to walk about so that any solution which might have entered the deep venous system can be rapidly carried away.

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A STUDY OF DERANGEMENT OF SEMILUNAR CARTILAGES BASED ON 850 CASES

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MENISCAL derangements are today well understood in most of their important phases. The causes of derangements, the clinical findings, and the types of injured menisci are well defined. There is general agreement on the treatment of the lesion, and the fact is well established that operative excision of the semilunar cartilage is a highly satisfactory procedure. In adding to the accumulated data on the subject, it is the writer's purpose: (1) to present a study of derangements that is based on an experience in this field extending over 30 years; (2) to analyze the findings and end-results in 850 cases that were treated surgically; and (3) to discuss the factors that affect the duration of the convalescent period and the success of operative excision of the cartilage.

ETIOLOGY

A derangement of the meniscus is usually the result of an injury in which the femur is suddenly twisted inward while a person is bearing his weight on the flexed knee, with the lower leg fixed in the position of external rotation. Participants in sports, and particularly in strenuous sports such as football, basketball, and skiing, are exposed to this type of injury, and hence in the younger age group from 18 to 28 the lesion practically always is the result of athletic endeavors. Older people, and especially those with an arthritic background, are likely to twist the knee in minor injuries such as in slipping on a waxed floor or a wet pavement or on the ice. The older person is not unlikely to sustain an injury to the cartilage while at work, particularly if the occupation necessitates holding the knee in a flexed position.

Undoubtedly, a predisposition to the lesion exists if there is any joint laxity. This may be the result of poor musculature, or of the weakening of the ligamentous structure from intermittent effusion in the joint, or of repeated occupational trauma. Static disturbances such as genu varum and flat feet produce a strain on the knee that makes the cartilage more vulnerable to injury.

Disease of a subacute or chronic nature is sometimes the underlying cause of a meniscal derangement. The lesion may be found in the presence of arthritis or of tuberculosis. In such cases it may be difficult to estimate the degree of the cartilage pathology, and the history and clinical findings as well as the duration of the symptoms must be considered carefully.

In a small percentage of cases the origin of the cartilage lesion is difficult to explain, the patient recalling no injury and the history being negative as to disease. Some authorities have advanced the theory that a degenerative process may be the underlying factor in such cases, and that tears in a cartilage are, in fact, sequelae to such a process. It is highly probable that in such cases there was a minor injury, one so slight as to pass unnoticed, and that the primary tear gradually enlarged until, upon only a slight twist of the joint, the cartilage was displaced.

AGE AND SEX

Cartilage derangements are most common among men between the ages of 18 and 40 years, which is the period of greatest activity in life. In recent years the ratio of females to males has shown a slight increase, due to women's activity in sports. The lesion is seldom seen in old age or in childhood, although defects of the external cartilage, due to congenital malformation rather than to trauma, are being recognized more frequently in the younger age group.

PATHOLOGY

Frequency of involvement of the internal cartilage. Lesions of the internal cartilage predominate over those of the external, the

Fig. 1.

Fig. 2.

Fig. 3.

Fig. 1. The cartilage split in trouser-like fashion.
Fig. 2. A bucket-handle fracture of the cartilage.
Fig. 3. A variety of bucket-handle fracture in which the loop of cartilage is turned over.

greater frequency being generally explained on an anatomical basis. The internal meniscus is a less mobile structure than the external, due to its relation to the internal lateral ligament and to its firm adherence to the articular capsule. Hence, in sudden rotation of the thigh, the internal meniscus is likely to be jammed between the articular ends and thus torn. The external cartilage, on the other hand, having attachments that are more lax, tends to escape the compression force of the articular surfaces, and to slip back into position uninjured following rotation strains of the knee.

Types of injured cartilages. The types of injured cartilages that are recognized as characteristic, although there is diversity of opinion as to the relative frequency of each type, may be classified as follows: fractured or torn cartilages—"bucket-handle" cartilages, hypermobile cartilages, congenital discoid cartilage.

A *fracture* of the cartilage is a common finding. Any part of the cartilage may be torn. The split may be longitudinal, transverse, oblique, or a combination of the longitudinal and the transverse. The longitudinal tear may be complete, running from the anterior to the posterior end of the cartilage, or it may be incomplete, splitting the meniscus in a trouser-like fashion (Fig. 1). Another type of tear is the "bucket-handle" fracture in which the inner loop of the torn cartilage swings into the joint-space (Figs. 2, 3, and 4).

The separation of a tag-like piece of the cartilage may take place at any part of its periphery. Figure 5 shows the anterior end of the cartilage detached, and a tag-like flap has been folded back toward the center of the joint.

The *hypermobile cartilage* is not uncommon and must be recognized as a genuine entity. It is the result of abnormal laxity of the meniscus at its perpiphery from damage to the capsular attachments. Undoubtedly marginal tears are associated more often with the hypermobile cartilage than is usually demonstrated.

Complicating pathology. The cartilage in addition to being fractured or loose is commonly found to be thinned or thickened, calcified, frayed, cystic, or showing degenerative changes.

Associated lesions are common. Almost without exception the infrapatellar fat pad is found congested and hypertrophied, with little tongue-like projections. The crucial ligaments, in particular the anterior ligament, are often found considerably engorged, or stretched, or even partly torn. Not unusual pathology in the crucial ligaments is a shredding of their attachments. Damage of the

Fig. 4.

Fig. 5.

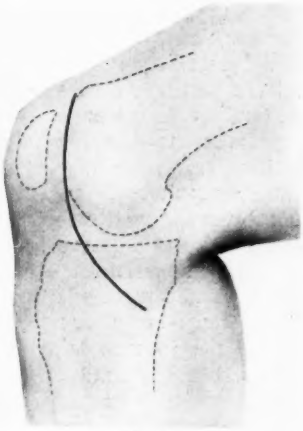

Fig. 6.

Fig. 4. Lateral view of the fracture shown in Figure 3.
Fig. 5. Detachment of the anterior end of the cartilage. The tab has been folded back toward center of joint.
Fig. 6. Line of incision.

lateral ligaments, and fractures of the patella, the spine of the tibia, or of the joint surfaces occur in conjunction with a cartilage derangement, but are uncommon. Loose fragments of articular cartilage may be present. There is *always* hypotonia and atrophy of the quadriceps extensor muscle.

In cases of long standing, the synovial membrane is red and swollen, and there may be villous changes in the synovial capsule. The articular cartilage may be covered with a pannus and show eroded areas. Hypertrophic changes may be present in the joint as the result of constant irritation from the damaged cartilage.

The congenital discoid meniscus. This type of cartilage represents a lack of normal development. It appears to be peculiar to the external meniscus, although cases of abnormal development of the internal cartilage as well as bilateral malformations have been observed. The form assumed by the cartilage varies widely; in some cases it persists in its fetal shape of a complete disc, and in others it persists as a disc with an open center over which is spread a thin curtain of tissue.

SYMPTOMS AND DIAGNOSIS

The patient, who is usually between the ages of 18 and 40, presents a typical history of injury, at the time of which acute pain was experienced and not infrequently a feeling that the knee gave way. In many cases it was impossible to straighten the knee after the injury, or bending was possible only after someone had pulled on the leg.

Unless the locking of the joint, which causes acute disability, forces the patient to seek medical attention promptly, he experiences several definite attacks of such giving way of the knee before consulting a physician. These attacks vary in severity, but usually they become increasingly mild and clear up more quickly. The patient, however, suffers constantly from the fear that the knee may give way at any time. If the knee remains untreated over an extended period of time, disability increases as the result of repeated damage to the joint in recurrent slippings.

The most dependable diagnostic features are the history of the injury; recurrent attacks of slipping of the knee associated with a feeling of insecurity at all times; intermittent effusion; pain and tenderness in the region of the offending cartilage; atrophy of the quadriceps extensor; and particularly the absence of the cartilage-thrust.[1] Locking of the joint,

[1]The presence or absence of the cartilage thrust may be determined by extending the knee joint. In the normal knee, when the joint is extended, the cartilage may be felt to bulge or thrust outward between the articular surfaces; this thrust is missing when the cartilage is torn and displaced in the joint space.

when present, is an important diagnostic sign. Tenderness may be elicited in the joint-line over the cartilage involved, and there is usually local thickening. The presence or absence of the cartilage-thrust can be determined by extending the knee.

It is not possible, as a rule, to make an accurate preoperative diagnosis of the type of injured cartilage from the clinical findings, although at times the symptoms are presumptive of certain pathology. Locking of the joint is indicative of a tear of the cartilage with displacement of a torn segment. When the damaged meniscus is of the bucket-handle type, the symptoms tend to be unusually severe at first, fluid persists in the knee, and the capsule becomes thickened. In cases of hypermobile cartilages, or of the detachment of one end of the meniscus, a sense of weakness only may be experienced. On the other hand, the symptoms may be misleading, since the attacks may be severe when the cartilage is of the hypermobile type, and mild when the meniscus is fractured. Again and again, the writer has been surprised to find an extensive pathological process upon exploring a joint that has given mild, although persistent, symptoms. For example, when the cartilage is completely torn at its periphery with only a rim remaining, mild symptoms may persist, and only when the meniscus is caught between the articular ends as the result of working the knee hard, do the symptoms increase in severity. Occasionally the symptoms may be indicative of involvement of the internal cartilage, but upon operative interference the external is found to be damaged.

When a child experiences symptoms that are suggestive of an external derangement, the presence of a congenital discoid cartilage should be considered. A history of trauma is not always recorded in these cases. The characteristic symptom of a discoid cartilage is an audible click in the outer margin of the joint, which is produced when the knee is in certain positions and especially as the leg approaches full extension. This symptom may be noticed by the parents soon after birth, but usually it becomes apparent later in life when the child is active. The discoid cartilage may persist without causing any particular symptoms or discomfort until an injury supervenes. On the other hand, there may be no history of an injury and yet the child, after a period of years, experiences intermittent attacks of pain accompanied by effusion and even by locking. Following a trauma the symptoms of a discoid cartilage are those of the usual derangement of traumatic origin.

In cases of suspected damage to a cartilage, roentgenograms of both knees in the anteroposterior and lateral planes should be obtained, not that they are of any diagnostic value unless the cartilage happens to be calcified, but they are essential to excluding concomitant lesions. Some observers claim to be able to demonstrate the injured cartilage by injecting various contrast media into the joint, and others recommend arthroscopy, but the results of such demonstrations are as yet inconclusive.

DIFFERENTIAL DIAGNOSIS

Loose bodies. If a loose body can be palpated, or visualized in roentgen films, there is no difficulty in distinguishing it from an injured semilunar cartilage. In other instances the symptoms of pain, swelling, and locking to which loose bodies give rise may be confusing. The locking, however, tends to be momentary, occurring whenever the loose body moves into the joint-space and acts as a block, and the pain on various lockings is referred to different parts of the knee.

Involvement of the infrapatellar fat pad. When the infrapatellar fat pad is enlarged, it may be pinched between the femur and the tibia upon extension of the knee, and even prevent complete extension at times. This pinching is accompanied by symptoms that simulate a derangement of the cartilage. Differentiation is not difficult, as a hypertrophied fat pad is palpable and slightly tender on pressure, and subpatellar crepitation is usually present.

Arthritic joints. In arthritic joints, the pain and swelling, and at times the pinching of fringes, are confusing symptoms. Roentgen films readily show any irregularities in the contour of the joint, and the history of a gradual onset of symptoms is indicative of arthritis rather than of a cartilage derangement.

Crucial ligament injuries. The diagnosis of a torn crucial ligament presents no difficulty, and can be distinguished with certainty by the presence of abnormal anteroposterior motion in the knee (a shuck).

Injury of the internal lateral ligament. Tenderness and pain in these injuries are localized on the medial side of the knee, and they are increased upon abduction of the leg. Lateral movement is abnormally free. The joint is never locked, and other signs of a cartilage derangement, such as the absence of the cartilage-thrust, are lacking.

Bone injuries. Such injuries as a fracture of the spine of the tibia, or a fracture of the patella without separation, can be differentiated from cartilage lesions by roentgenographic examination. In severe injuries of the knee, however, the meniscus is likely to be damaged, and the symptoms of a derangement appear later following the treatment of the fracture.

TREATMENT

Treatment of derangements of traumatic origin. The treatment of cartilage lesions is based to a certain extent upon an understanding of the repair process in a damaged meniscus. The semilunar cartilages have a limited blood supply, the peripheral zone being vascular, whereas no blood vessels can be traced in the body of the cartilage. True repair of a split or tear may be expected only if the damage lies in the vascular area. Since it is not possible by physical examination to determine the site of the pathology, and because the injured cartilage might be of the simple hypermobile type, primary derangements are given the benefit of conservative treatment for at least several weeks, unless the case is obviously surgical.

Conservative treatment. The treatment should be carried out promptly. Injuries that appear to be slight should not be neglected. If there is excessive fluid, the joint may be aspirated.

When there is no locking, the joint is immobilized in the position of extension. For this means a flannel bandage that extends from the mid thigh to the mid calf, or a posterior plaster shell, or a ham splint may be used, the type of retentive dressing depending upon the severity of the injury.

If locking with displacement of the cartilage is present, immediate reduction before the repair process sets in is important. There are several effective methods of reduction, among which is that of Jones (16). This method consists of first flexing the knee sharply, then rotating it and moving it sideways to open the joint-space, and finally extending the leg completely. Following the reduction the knee is immobilized in the position of extension as is done in cases in which there is no displacement.

Upon the subsidence of the acute symptoms, which usually takes place within 2 or 3 days, the patient should begin practicing contraction of the quadriceps muscle. Baking, massage, and gentle passive motions are started in a week or 10 days. Walking with the aid of crutches may be started in a few days when the patient is comfortable, the active use being extremely beneficial in easing pain, helping to reduce the swelling, and preventing muscular atrophy.

The period of immobilization varies with the severity of the injury. As a rule, the bandage or splint may be removed in 3 weeks, but if any fluid persists, the joint must be protected longer. No weight should be borne until the fluid has subsided. Any strain on the internal lateral ligament is prevented by raising the inner side of the sole and heel of the shoe, in order to force the patient to walk with the foot in the position of inversion. The patient should make a conscientious effort to improve the tone of the thigh muscles by practicing contraction exercises.

Operative treatment: Indications. A severe derangement of the semilunar cartilage with displacement that proves to be irreducible by manipulation calls for immediate operative interference. Recurrent cases with a history of attacks of slipping followed by pain and tenderness, and unrelieved by conservative treatment, must be treated surgically. The removal of the cartilage should not be postponed in recurrent cases because of the danger of weakening the joint structures through the intermittent effusion, and because of the likelihood of the development of arthritic changes in the presence of defective mechanics of the joint.

When the cartilage derangement is complicated by arthritic changes in the knee, the indications for operation must be considered carefully. The age of the patient; the nature of the arthritic process, that is, whether it is local or generalized; and whether the disability is due to the cartilage derangement or to the arthritic process are all factors that must be weighed. In the presence of progressing symptoms that are clearly due to a damaged cartilage, prompt operative excision of the meniscus is indicated, unless definite contraindications to any operative interference are present.

Preoperative care. Even before the operation, particular attention should be given to recovering good tonicity of the quadriceps extensor muscle upon which the stability of the knee so largely depends. In the average case of derangement this muscle shows a lack of tonicity within a few days after receipt of the initial injury. The patient while he is waiting to enter the hospital should practice voluntary contractions of the quadriceps, for from 100 to 200 times, every hour that he is awake.

Operative technique. A careful 2 day preparation of the operative field and rigid aseptic technique are essential to successful arthrotomy. The leg from the ankle to the groin is shaved, then washed with soap and water for as long as 10 minutes, and scrubbed with alcohol and ether. On the eve of the operation, the same field is painted with 3 per cent iodine, the leg held elevated until dry, and a sterile dressing applied, which is not removed until the time of the operation. Just before the incision is made the area is again painted, this time with 7 per cent iodine.

A tourniquet is applied to provide perfect hemostasis and to prevent postoperative hemorrhage. The knee is properly draped and flexed to the right angle over the edge of the operating table. A sterile towel is laid over the joint, through which the line of incision is imprinted. The towel is then removed.

The routine incision, in the case of a derangement of the internal cartilage, begins over the upper edge of the femoral condyle and curves downward over the inner border of the tibia (Fig. 6). When the external cartilage is involved, a similar incision is made over the outer condyle. If the symptoms and signs suggest that both cartilages may be involved, or if the injury is so severe that complicating pathology is undoubtedly present, a wider incision that permits the exploration of both cartilages and the entire joint is used. The general use of a wider incision, however, is unnecessary, as is proved by the rare recurrence of symptoms in a large series of cases in which either the smaller internal or external incision was used.

In the case of involvement of the internal cartilage, the operative procedure continues as follows: The surgeon, using a fresh knife, incises the fascia, the internal lateral ligament, and the capsule, making the incision of sufficient size to expose the cartilage. The damaged meniscus is then removed in its entirety, regardless of the amount or the location of the pathology. There may be cases of simple detachment of the anterior extremity of the cartilage, with the posterior segment remaining attached, in which excision of the damaged portion alone will prove satisfactory, but there is always the danger that a tear of the posterior part has been overlooked or that one may occur. In the case of the bucket-handle type of fracture the removal of the detached loop alone, as recommended by some operators, may prove unsatisfactory because of pathology in the remaining marginal section.

Tension is kept on the cartilage while it is being removed. The anterior part is first freed, and then the operator holding this end of the cartilage under tension by means of Ochsner snaps dissects the remaining portion from its attachments. The posterior section is severed by means of scissors so fashioned that they conform to the contour of the tibial tuberosity. In order to make the dissection easier, the tibia may be rotated or a blunt dissector may be pried between the articular surfaces. Care must be taken not to damage the articular cartilage in removing the meniscus.

The interior of the joint is then inspected thoroughly, and any other pathological condition noted. This step in the operative procedure is of extreme importance. If the articu-

lar cartilage is frayed, eroded, or degenerated, it should be trimmed until normal cartilage is encountered. Loose bodies should be removed, and in order to make certain that none are overlooked, the joint should be explored with the gloved finger. A hypertrophied infrapatellar fat pad should be excised. Large bony spurs which are the result of arthritic changes should be removed. The crucial and lateral ligaments should be inspected, although the damage is seldom so severe that repair is necessary.

Attention is now given to closing the wound. The capsule and internal lateral ligament are sutured with interrupted fine catgut. The fascia is closed with continuous catgut No. 2, and the skin with silk. A sterile dressing is applied, extending from the mid thigh to the toes, with the leg held straight. A snugly fitted flannel bandage is finally applied, extending from the mid thigh to the toes, with moderate compression over the knee. Only at this time, when compression has been applied, is the tourniquet removed, thereby preventing any postoperative effusion and oozing into the joint.

Postoperative care. Most important in the after-care are the preservation and improvement of the tonicity of the quadriceps extensor muscle. As soon as the patient is comfortable, contractions of the quadriceps should be practiced hourly during the day, from 100 to 200 times. In about a week or 10 days the patient may get up and start walking with the aid of crutches. The compression bandage is worn for from 10 days to 2 weeks, and upon its removal, baking and massage and gentle passive motions are begun. In about 3 weeks the patient should be able to bend his knee to a right angle, and in from 4 to 6 weeks to return to moderate activity.

Treatment of the congenital discoid cartilage. A suspected congenital discoid cartilage in the child is left untreated if it causes no discomfort or disability, although in cases of recurrent snapping there is the possibility that arthritic changes may develop. On the other hand, when the patient experiences attacks of pain or is in any way handicapped by the presence of such a cartilage in the knee, operative excision is indicated.

In the treatment of a suspected congenital meniscus with a superimposed injury, the surgeon is guided by the relation of the trauma to the symptoms. In a knee that has had a definite click and in which the symptoms have been aggravated by trauma, operative removal of the cartilage is advisable. In the treatment of patients who have no history of snapping, conservative measures are first adopted.

ANALYSIS OF CASES

The series of 850 operative cases to be discussed were treated over the 37 year period from January, 1904, to December, 1941. A review of 388 of these cases, which had been treated in the 25 year period from 1904 to 1930 was published in 1931.[1] Owing to the fact that data are sometimes missing from clinical records, it has not always been possible to report findings in all 850 cases.

Sex, age, and knee involved. Of the 850 patients, 541, or 64 per cent, were males. In recent years, the ratio of females to males showed a slight increase, a variance that may be due to women's increasing activity in sports.

The ages were recorded in 786 of the 850 cases. At the time of the operation, 405 cases, or approximately 50 per cent, were between 20 and 40 years of age, the larger number (251) falling into the age group between 20 and 30 years. In the age group between 10 and 20 years, there were 172 cases; and in the group between 40 and 50 years, 107 cases. Only 6 patients were under 10 years of age, and only 27 were over 60.

There was only a slight difference in the number of cases from the standpoint of the knee involved. There were available 820 records, and of this number 428 were derangements of the right knee, and 392 were of the left knee.

Causes. By far the majority of young people had injured the cartilage while active in sports, and practically every sport was represented, with football, basketball, and skiing holding prominent places. In a large percentage of the older age group, a fall had been the responsible factor, in particular falls on the

[1]Ann. Surg., 1931, 93: 649.

ice or on wet floors or pavement. In a small proportion of cases the knee had been injured in an automobile accident.

Disease was the underlying factor in 5 cases, tuberculosis being the cause in 1 case, and hypertrophic arthritis in 4 cases.

In several cases the patients reported that the cartilage had slipped without apparent cause, the onset being sudden in some cases and gradual in others.

Duration of symptoms. The period of time that had transpired between the initial attack and the date of operative intervention ranged from the minimum of a few days in 6 cases to the maximum of over 30 years in 3 cases. By far the majority of patients had experienced recurrent attacks for months or years, and the larger proportion of these had had symptoms for from 1 to 5 years. The time lapse in the 768 cases in which this factor was recorded was as follows: a few days, 6 cases; 1 to 3 weeks, 85 cases; 1 to 10 months, 260 cases; and 1 to 30 years, 417 cases.

Surgical pathology. Lesions of the internal cartilage predominated over those of the external, the ratio of injuries of the former to those of the outer meniscus being 6 to 1. Both cartilages in the same joint were involved in 124 cases. No data on this finding were available in 43 cases.

Owing to the fact that more attention has been given to recording the exact pathology in recent years, the data on the type of damaged cartilage and the nature of the associated pathology are more complete in the later series of cases than in that published in 1931. In the earlier series of cases (435 cartilages), the hypermobile cartilage held a prominent place, 146, or 34 per cent of the damaged cartilages being recognized as of this type. Undoubtedly, fractures existed in many of these cases, but they were overlooked or were not mentioned in the records. Tears were found to be present in 149 cases, but the site and type of fracture were noted in only a few instances.

In the later series of 462 cases (539 cartilages), fractures were demonstrated in 303 instances. The greater number were located in the posterior part of the cartilage, and the next most frequent site of involvement was the anterior end. Splitting of the cartilage in trouser-like fashion, and tears running the entire length of the cartilage from its anterior to posterior end were common. The bucket-handle fracture was present in 47 cases. The hypermobile type of cartilage was found in 158 of the 539 cases. There were 4 cases of a congenital discoid meniscus. Six cartilages were cystic; 1 was calcified; 1 was missing entirely; and 32 were thinned or thickened. In 34 cases the pathological process was not recorded.

Lesions of other joint structures were associated with the damaged cartilage in many instances. In the later series of 462 cases, the most common complications were arthritic changes, 56 cases; damage of the crucial ligaments, 51 cases; erosion of the articular cartilage, 13 cases; and loose bodies of bone or cartilage, 24 cases. Less frequent concomitant lesions were fractures of the patella, 1 case; fractures of the spine of the tibia, 7 cases; fractures of the tibial tuberosities, 9 cases; and fractures of the femoral condyles, 5 cases.

End-results. Questionnaires were sent to 842 of the 850 patients. Inquires were not sent to the other 8 patients because of the fact that the presence of serious complications at the time of the operation would preclude judging the outcome of the surgical procedure. In this group were the following: 1 case of postoperative sepsis; 1 tuberculous knee; 1 Charcot joint; 3 cases of generalized arthritis; 1 severe fracture; and 1 case of intermittent hydrops.

The patients were questioned on the following points: (1) their satisfaction with the operation, (2) the amount of motion in the knee, (3) the stability of the knee, (4) the comparative strength of the two knees, and (5) the time lapse before activity was resumed after the operation.

Replies were received from 656 patients. In these cases the time interval between the operation and the postoperative check was as follows: 5 to 10 months, 9 cases; 1 to 10 years, 511 cases; and 10 to 25 years, 136 cases.

Five hundred and forty of the 656 patients who returned the questionnaires expressed satisfaction with the outcome of the operation. All of the patients had resumed their normal

life and returned to their regular occupations including nursing, trucking, teaching, dancing, carpentry, and the heavy industries. Twenty-seven patients were in the Army, 6 in the Navy, and 4 in the Air Corps. Many engaged in strenuous sports. The majority of the "satisfied" group had resumed activity in 3 months after the operation.

Approximately half of the group claimed some slight disability or discomfort, although they were able to continue their work and participate in sports. Most serious was a slight limitation in motion, especially in flexion, in 142 cases. Several patients (78) experienced a feeling of instability at times, as after considerable walking or exercise, or in running, or in going up or down stairs. Several (149 patients) reported that the knee operated upon was weaker than the normal joint so that they tended to favor it. Thirteen patients complained of pain in damp or stormy weather. In this group of cases, factors such as the complication of arthritis or damage of the crucial ligaments, or the question of litigation, must be considered in weighing the patient's opinion as to the outcome of the operative excision of the cartilage.

Forty-nine patients replied that they were only partly satisfied with the result. Some complained of a limitation of motion, weakness, and instability; others experienced only a sense of weakness; and still others claimed a recurrence of the symptoms of a deranged cartilage. These patients were asked to report for an examination of their knees. In only 7 of the 49 cases could the results be considered unsatisfactory from the surgeon's standpoint. In 8 cases the cartilage had been removed in the presence of coexisting arthritis, and several of these patients had suffered from a slipping cartilage for years before the operation. In 3 cases there had been damage of the crucial ligaments. Seven patients had a persistent weakness of the quadriceps muscle. One patient had had a fractured hip on the same side as the deranged cartilage; 1 had sustained a new injury and damaged the other cartilage; 1 had had an ulceration, but healing was satisfactory; and in 1 case there had been an inflammatory reaction in the synovial sac that precluded a good outcome from the cartilage operation. Four patients were seeking additional compensation from insurance companies. In the 16 remaining cases there appears to be no explanation of the patient's unfavorable opinion, as several of the patients were active in such sports as skiing and soccer;

SUMMARY OF 850 CASES—541 MALES, 309 FEMALES

Age—years	Number
4 to 10	6
10 to 20	172
20 to 30	251
30 to 40	154
40 to 50	107
50 to 60	69
60 to 75	27
Unrecorded	64
Knee involved	
Right	428
Left	392
Unrecorded	30
Duration of symptoms before operation—	
Days	6
Weeks—1 to 3	85
Months—1 to 10	260
Years—1 to 30	417
Unrecorded	82
Cartilage involved—	
Internal	591
External	92
Both	124
Unrecorded	43
Pathology—	
Early series, 435 cartilages	
Hypermobile	146
Fractures	149
Dislocations	50
Totally avulsed	5
Unrecorded	85
Later series, 539 cartilages	
Fractures	303
Hypermobile	158
Congenital discoid	4
Unusual pathology	40
Unrecorded	34
End-results—842 questionnaires	
From patient's standpoint—	
Good	540
Partly satisfactory	49
Unsatisfactory	67
No replies	186
From surgeon's standpoint—	
Good	614
Partly satisfactory	7
Poor	26
Satisfactory in 186 "no reply" group	32
Unclassified	13
No replies	150

1 was a foreman and stood on his feet for 12 hours a day; 1 patient, aged 50 years, had only the complaint that he could not squat; and a boy claimed that he had symptoms, but his mother wrote that the knee was perfectly satisfactory.

Sixty-seven patients were definitely dissatisfied with the outcome of the operation. Upon investigation of these cases, it was found that from the surgeon's standpoint only 25 were poor results. Eighteen patients claimed a recurrence of the slipping of the knee, and although several of them refused to report for examination, it must be assumed that pathology in the form of a derangement of the other cartilage, a loose fringe, or an enlarged infrapatellar fat pad was present. One knee became septic. Two patients complained of constant pain; 1 had an unstable knee; 1 a stiff knee; and 1 experienced instability and pain. In 1 knee there was a beginning dissecans.

The results in 10 cases could not be classified. Two patients had injured the knee shortly after the operation; 1 had a blood stream infection; 1 a Neisserian infection; 1 a tuberculous knee. There was an osteochondritis in 1 knee. Two knees had been so severely injured that it was impossible to judge the outcome of the excision of the cartilage. One patient left the hospital against advice, and 1 patient consulted an osteopath.

In the remaining 32 of the 67 cases, the result of the operation itself was satisfactory, the symptoms of the deranged cartilage being relieved and the joint generally improved. In these cases, the presence of such complicating factors as arthritis, crucial damage, and persistent weakness of the quadriceps were responsible for the condemnation of the operation.

In the group of 186 patients from whom no replies were received, an attempt was made to judge the result from the patient's record, and in 36 cases examinations had been made after a sufficient time to permit classifying the outcome. There were 32 good results in this group, 4 of which were complicated by an arthritis and 1 by weakness of the quadriceps muscle. Three cases could not be classified because of the severity of the initial injury in 1 case and because of a nervous element in 2 cases. One knee became septic.

Summary of end-results. In this series of 850 cases, conclusions on the end-results are based on 692 cases, including the 656 replies received from questionnaires that were sent to the patients, and 36 cases on which it was possible to judge the outcome from the clinical records. Whereas only 540 patients expressed complete satisfaction with the outcome of the operation, a careful investigation of these cases showed that 646, or 90 per cent, obtained good results from a clinical standpoint. In 7 cases results were partly satisfactory; in 26 they were poor; and 13 results could not be classified.

PROGNOSIS AND FACTORS AFFECTING OPERATIVE RESULTS

From the standpoint of both the patient and the surgeon the operation for excision of a deranged meniscus is a highly successful procedure. The average patient, if treated promptly upon the recognition of the lesion, obtains a knee that is stable, painless, and has complete function. The patient is usually able to return to office work within a few weeks and to strenuous occupations in from 2 to 3 months.

Unsatisfactory results following the operative removal of the cartilage, as well as a prolonged convalescence, may be traced either to one of several factors or to a combination of factors.

Arthritic changes. The prognosis is not so favorable, and a longer convalescence may be expected in patients in whom an arthritic process or hypertrophic changes are present in the joint at the time of operative intervention. It is well to make the patient acquainted with this fact before the operation is undertaken. In elderly patients these changes may be of a chronic nature involving several joints, and the cartilage may, in fact, be damaged by the compression of a flat, eburnated condyle. Arthritic changes may also be present in the knee of the young adult, as well as in the joints of older patients, when the cartilage derangement has been of long standing. Such changes are provoked by the repeated trauma to which the knee is subjected and also by

the presence of defective mechanics in the joint.

Arthrotomy in cases complicated by arthritic changes may give relief from the symptoms directly traceable to the cartilage derangement, and some functional improvement may be obtained as well as the prevention of further arthritic changes. A less satisfactory outcome must be expected, however, as the removal of the cartilage in no way affects the arthritic changes which are already present, and the knee must always be protected and favored.

Persistent traumatic synovitis and relaxed ligaments. Repeated trauma with effusion may lead to chronic synovitis and a weakening of the ligamentous structure of the knee-joint, complications that may be responsible for a persistent weakness following the removal of the meniscus. Such a complication may be avoided by early operative interference and by improving the tonicity of the quadriceps muscle through the practice of regular contraction exercises.

Associated pathology. Injuries of the cartilage are often complicated by damage of other joint structures, which affects the ultimate result of operative excision of the cartilage. A not uncommon lesion is damage of the crucial ligaments, which may give rise to a persistent laxity of the joint following the removal of the cartilage. In such cases, the best treatment consists of measures to improve the muscular structure.

Erosion of the articular cartilage is another common finding at the time of operation, which may prevent obtaining a perfectly satisfactory joint, although the symptoms from the cartilage derangement are eliminated.

Finally, in the presence of such severe injuries as fractures, it is to be expected that the knee in certain cases cannot be restored to normal.

Weakness of the quadriceps extensor muscle. A most important factor affecting the outcome of a meniscus operation as well as the duration of the convalescence is a persistent weakness of the quadriceps muscle. In such cases, the patients complain that the knee operated upon is slightly weaker or less stable than the normal knee, or that it tires more easily, or gives trouble in going up and down stairs, in running, or in exercising. The symptoms may be present in cases that have been treated either soon after the initial injury or following recurrences of slipping of the cartilage.

This lack of tone in the quadriceps which accompanies injuries of the knee joint is not due to disuse entirely, because it develops in some cases within a few days after the initial trauma. The more prolonged the symptoms of a derangement, the more severe are the hypotonia and atrophy of the muscle, and in such cases a long period of time may be required to restore the normal tone.

In view of the extreme importance of the tonicity of the quadriceps extensor to the stability and function of the knee, particular care should be taken to maintain its tone throughout the course of treatment. It should be particularly impressed on the patient that he must co-operate fully in order to recover this muscle power.

CONCLUSIONS

A study of derangement of the semilunar cartilages is presented, which is based on an experience in this field that extends over more than 30 years. An analysis of the findings in a series of 850 cases is reported. Examination of the end-results in this series of cases showed that 90 per cent of the patients obtained satisfactory results from a clinical standpoint.

The factors that may interfere with obtaining a good outcome by operative intervention are discussed, among which are the presence of arthritic changes or associated pathology in the joint, and the persistent weakness of the quadriceps extensor. Emphasis is placed on the importance of prompt and effective treatment of cartilage derangements in order to prevent the development of arthritic changes, and to preserve and develop the tonicity of the quadriceps muscle.

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ROENTGEN PELVIMETRY

A Commentary

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THE perfection of roentgen techniques to furnish definite information concerning pelvic capacity has demonstrated with certainty the inability of ordinary external pelvimetric methods to secure such knowledge. At best these latter methods can give but a general idea of available pelvic space, and experience has shown that at times information so obtained may be even misleading. It is obvious that if the knowledge of pelvic dimension and pelvic conformation is useful in obstetric procedure, then such information should be as complete as necessary and of reasonable accuracy. It can hardly be questioned that such knowledge is useful, for a greater part of the problems associated with labor are in the nature of a mechanical art, and as Rongy has stated: "The obstetrician like the engineer must guide himself wholly in accordance with the principles which make a given mechanical problem safe or unsafe, possible or impossible." However, it must not be forgotten that, useful as is this knowledge of pelvic dimension and pelvic conformation, the bony pelvic canal is but one important part of the rather complicated labor mechanism and, bearing this in mind, the statement of Dippel regarding roentgen pelvimetry is of particular interest. He writes: "It may be argued that there are so many factors in labor, namely the size of the baby and the character of the uterine contractions, that an approximation is enough. We do not agree with this viewpoint. The fact that these other factors are difficult to evaluate accurately makes it all the more important, in cases of contracted pelvis, that we should have as precise information as possible concerning the one factor we can measure with precision."

Because of the definite clinical significance of variations in the bony pelvis the experience of the writer has led him to go beyond this and to recommend that all primigravid women should have the benefit of the roentgen survey of the pelvis. During the past 7 years this has been done in our clinic and nearly 2,000 patients have been so surveyed. The results have been convincing, for not only have been discovered numerous unsuspected pelvic anomalies but clinically significant pelvic variations have been noted that otherwise would have remained undetected. In this connection the statement of an eminent British obstetrician is pertinent. In 1939 J. M. Munro Kerr wrote: "I do not think that, with the knowledge now at hand regarding the influence excited even by minor variations of pelvic conformation, we who advocate routine pelvic radiography for all primigravidae have lost our sense of proportion in this matter as many suggest today. On the contrary, I make bold to predict that before many years pass it will be accepted as an essential detail of the antenatal examination."

The chief purpose of the present communication is to comment generally upon this subject, drawing upon an experience now extending over two decades and hoping that these observations will be helpful to those who are interested in the practical application of roentgenometry to clinical obstetrics.

1. By the term "roentgen pelvimetry" we include a roentgen visualization of the pelvis in which not only pelvic measurements may be made but important pelvic contours may be studied.

2. Any method of roentgen pelvimetry to be generally useful must be simple, accurate, inexpensive, and capable of ready interpretation by those engaged in the practice of obstetrics.

3. Roentgen pelvimetry should be done during pregnancy and the results incorporated in the prenatal record. In this way will be accumulated a store of information which will

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enable us further to evaluate the clinical significance of pelvic variations and to establish average dimensions in certain groups. Apparently, the largest number yet reported from this point of view is the author's study of 1,100 white women published in 1941. In cases at term or in labor in whom disproportion is present or suspected, further roentgen studies should be carried out, but roentgen pelvimetry as here defined should be a prenatal procedure.

4. It should be emphasized that the responsibility for interpreting roentgen films belongs definitely to the obstetrician. However, it requires experience to evaluate these findings, for we must recognize the fact that previous to the use of roentgen techniques our knowledge of the bony pelvis in the living being was largely rudimentary. The obstetrician in interpreting roentgen films must possess a knowledge of the newer concepts of the pelvis from the obstetrical viewpoint. This can best be obtained from the ever-growing literature on this subject. The actual measurement and visualization of the pelvis with the techniques that we employ is almost as simple as viewing the dried anatomical specimen.

5. A more general adaptation of roentgen pelvimetry to clinical obstetrics has been somewhat delayed by the multiplicity of roentgen techniques that have been developed. This has come about because many investigators have endeavored to seek a degree of accuracy all out of proportion to that which is essential for clinical use. If one considers the entire obstetric pelvis, bones, soft parts, articulations, and the influence of pregnancy upon the latter, it is evident that any dimension of the bony pelvic canal which is accurate to 0.5 centimeter must be clinically satisfactory. In the simple methods which we have so long used with a target-film distance of 36 inches we are certain that any dimensional error is well under this figure.

6. The two pelvic views which we use in the routine survey are the inlet and lateral views. The use of the 36 inch target-film distance is an important point, for distortion is minimized at this distance and by using the same distance for each view one can be readily compared with the other, and certain dimensions thereby checked in each film.

7. The success of these simple techniques greatly depends upon the proper positioning of the patient. This is not difficult, but the roentgen technician must develop a certain amount of skill for good results. At this time it is not proposed to go into the technical details of these procedures, for they have been published fully elsewhere (4); however, a short description may be useful in this place. The inlet view (Fig. 1) is taken with the patient semirecumbent, using a back rest and centering the target 6 centimeters posterior to the upper symphysial border. We endeavor to make the pelvic inlet parallel to the film, and this may be accomplished by measuring vertically the distance from the table top to a point 1.5 centimeters below the upper symphysial border on its anterior surface and measuring vertically the distance from the table top to the interspace posteriorly between the 4th and 5th lumbar vertebrae. The patient's position must be such that these two points are equidistant from the table top, for they establish the level of the pelvic inlet. (Some observers have suggested that the sides of the inlet or iliopectineal lines in some cases may rest below this level and thus give an erroneous reading of the transverse diameter. Experiments with the dried pelvis and the *36 inch distance* have shown us that such error is unlikely and is minimal, if present at all.) The lateral view (Fig. 2) is taken with patient standing in the lateral position, the target being centered at the upper edge of the acetabulum. The correction of distortion in both views is made with an isometric rule introduced in the plane to be measured and thus appearing on the film. In the inlet view this is done by a double exposure and in the lateral view this scale is projected at the one exposure. A correction table, depicting values for various levels for 36 inch target-film distance, has been used by some investigators and there is no reason why it cannot be successfully used instead of this scale. However, having the correction directly on the film makes for simplicity in film interpretation.

8. In viewing the films there are certain portions of the pelvis which have particular

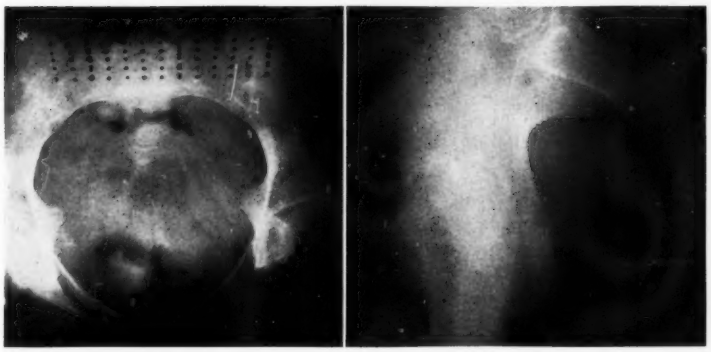

Fig. 1, left. Pelvic inlet roentgenogram. The top row of dots represents "corrected" centimeters for the level of the pelvic inlet. Interspinous and other lower level diameters are measured by using other series of dots which are calibrated for 5, 6, 7, 8, 9 centimeter levels below that of the inlet.

Fig. 2. Lateral pelvic roentgenogram. "Corrected" centimeter scale shown on one side of film. All anteroposterior pelvic diameters may be measured.

obstetrical significance. These are the planes of the pelvic inlet, midpelvis, and pelvic outlet. Any or all of these planes may show abnormal narrowing in one or more diameters. There are also certain contours of the pelvis which have obstetrical importance and a proper pelvic survey cannot be carried out unless both dimensional data and contour study are evaluated.

9. A word might be said concerning the time and expense involved in the making of these two roentgen views. We have found that an allowance for each patient of 15 to 20 minutes is sufficient. As these patients are ambulatory, appointments are made to suit the convenience of the Roentgen Department. The inlet view may be taken on an 8 by 10 film and the lateral on an 11 by 14. The complete cost is well within the range of ward patients to pay and is certainly at a cost-level in line with most clinical laboratory procedures.

10. We do not include pelvic outlet views in the roentgen survey. Roentgen methods are not too satisfactory for accurate mensuration in this portion of the pelvis and the usual palpatory methods are adequate for both mensuration and for determining the important contours. The chief dimension of clinical value is the transverse diameter of the outlet. This is taken at a level 5 centimeters below the inferior border of the symphysis. Because of a lack of definite end points when using a level lower than this, observers measuring this diameter rarely get consistent results. When we consider the course of the pelvic axis at the outlet and the fact that the suboccipitobregmatic diameter of the fetal head is approximately 10 centimeters, the use of a dimension level at 5 centimeters or the radius of the suboccipitobregmatic circumference seems a more rational and accurate procedure.

11. A brief word may be said concerning the influence of routine roentgen pelvimetry on obstetric procedure in general. Certain facts have become apparent in our comparatively extensive experience. Briefly these are: (a) The incidence of trial labor, a procedure which is subject to great abuse, has been lessened; (b) the incidence of the difficult forceps operation has also decreased; (c) the fetal mortality in primigravidae with breech presentation has definitely lessened; (d) it does not appear that routine roentgen studies tend to radicalism.

In 1100 primigravid white women consecutively delivered at term (child 2500 grams or over) our figures for major operative procedures are: cesarean section, 26 times or 2.3 per cent; version and extraction 5 times or 0.4 per cent; and midforceps 39 times or 3.5 per cent. Put in another way, 93.8 per cent of this group of primiparous women were delivered without resorting to any major op-

erative procedure. It should be obvious that a number of the above operations were done for indications other than cephalopelvic disproportion. In one group of patients it is certain that the roentgen survey has definitely decreased the incidence of cesarean section and that is in those cases of unengaged head in primigravid women at term, or even in early labor, where palpatory methods may have suggested apparent disproportion. In many of these cases roentgen pelvimetry has demonstrated ample pelvic space and shown that a conservative course could be safely followed.

12. In conclusion, we must agree that with the rapid increase in the incidence of hospitalization of obstetrical cases have come greater opportunities for the safe and scientific conduct of labor. In our experience the forehand knowledge of available pelvic space and of pelvic conformation, as shown by prenatal roentgen pelvimetry, has eliminated certain trial and error methods of obstetric procedure and placed operative measures on a sounder basis. The proper conduct of labor must always be carried out with the least possible trauma to both mother and child, and the roentgen survey of the pelvis is one of the measures which will greatly aid in realizing this desideratum.

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AORTIC EMBOLECTOMY

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WHILE there is doubt if some peripheral arterial embolisms (4) should be operated upon because of the tendency for collateral circulation to be adequate, there is no doubt but that complete obstruction of the bifurcation of the aorta from acute embolism should be operated upon. In a fair proportion of these cases, the immediate symptoms and signs suggest complete obstruction, but under observation for a few hours the findings change, indicating that what was originally impaction at the bifurcation of the aorta has changed, by the mass or masses, breaking and slipping down one or both sides to a lower level. In the cases, however, in which the evidence of aortic embolism persists for a few hours, if the general condition of the patient warrants, surgical removal should be attempted, otherwise the prognosis is fatal, with the result that in nearly all cases, the patients go through the painful stages of developing gangrene of both legs, and death from toxemia.

The descriptions in the literature (1, 6) and comments by surgeons seem to throw an atmosphere of awe and despair about such a condition. On the other hand, the technical procedure of removing such an aortic embolus is not difficult and, if undertaken within 12 to 20 hours after the accident and successfully completed, results are exceedingly gratifying and the prognosis is changed to one of optimism, provided the pre-existing cardiovascular disease has not in itself jeopardized the chances of the patient.

A report of 5 successful aortic embolectomies follows. In all 5 cases there were no technical difficulties and no accidents or disasters. The circulation was restored in all 5 cases and the impending gangrene of both legs in each case was immediately replaced by extremities with normal circulation and function, thus transforming the picture to that of the original healthy state.

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OPERATION

Several methods of approach have been studied and tried, but the one used in these 5 cases, which has been entirely satisfactory, has been through an extraperitoneal abdominal approach. The incision is a right paramedian, extending from 2 inches above the umbilicus to the symphysis pubis. The transversalis fascia is divided and care is taken not to open the peritoneum. An areolar plane between the peritoneum and transversalis fascia is easily followed by blunt dissection with the fingers and within a very short space of time the peritoneum is swept out of the right iliac fossa and retracted with the cecum and other intraperitoneal organs to the left side. Only two obstacles to this dissection are encountered. The first is the structure leaving the abdomen through the internal abdominal ring. In the male it is wise to dissect off the vas deferens and spermatic vessels from the peritoneum and leave them behind as the peritoneum is swept to the left side. In the female the round ligament is divided between ligatures. The ureter is the second organ to be protected. It must be reflected off the peritoneum as the latter is elevated and the ureter is left in its original position. When this has been accomplished, the external, internal, and common iliac vessels on the right side as well as the hollow of the sacrum are well exposed. The chief difficulty in the exposure is the separation of the peritoneum from the posterior rectus sheath and transversalis fascia above the level of the semilunar fold of Douglas, and this difficulty is increased above the level of the umbilicus. Over these areas, the peritoneum may be opened during dissection. However, this matters very little because with the retraction to the left, the intraperitoneal contents do not escape and are not in the way during the operation. As the peritoneum is dissected off these areas, the posterior rectus sheath above the semilunar fold of Douglas is divided to the level of the upper end of the skin incision. The dissection of the perito-

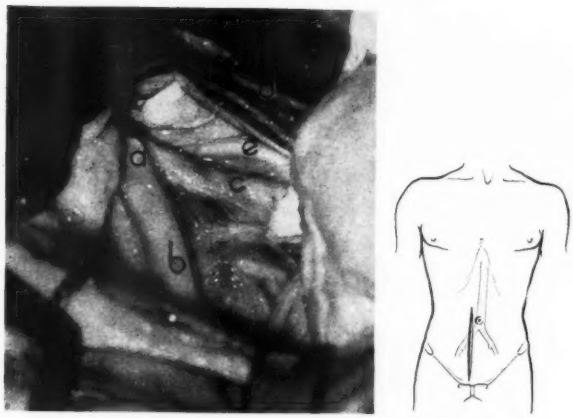


Fig. 1. Field showing retraction of peritoneum exposing: *a*, bifurcation of aorta, *b*, right common iliac artery, *c*, left common iliac artery, *d*, right ureter retracted over to left side of field, *e*, left ureter crossing lower end of left common iliac artery. Insert showing abdominal incision for approach to aorta.

neum to this point can be carried out within a very few minutes. When proper packing and suitable retraction are applied to this reflected peritoneum, the lower 3 inches of the abdominal aorta, its bifurcation, the left common, internal, and upper few inches of the external iliac arteries and veins as well as all those on the right side are exposed in the field.

At this stage, the level at which the pulsations disappear in the aorta and the absence of pulsations in the common and other iliac vessels will be obvious. As well, the firm mass obstructing the vessels can be palpated with the finger.

The next move is to discover the lower limits of the obturating embolus in both right and left external iliac vessels. When this has been defined, the areolar tissue around the vessels is separated so that a bulldog clamp can be applied distal to the mass on both right and left sides. The distal limits of the masses in both right and left internal iliac vessels may also be defined, and similar clamps applied here. This protects the circulation peripheral to this point, from smaller masses escaping during future manipulations. The next step is to define the circumference of the abdominal aorta about 1.5 to 2 inches above the bifurcation, at which point a length of surgical tape is passed around the aorta in the form of a loop. By twisting this tape gently and at the same time holding the gently twisted tape with the three inner fingers and by counter pressure with the index finger over the small remaining loop, the lumen of the aorta can be gently occluded temporarily. Great care must be exercised in handling this tape because the aorta is friable. A strong tug or jerk on this tape might do irreparable damage in the form of an immediate tear or, by damaging the intima, might precipitate thrombosis at a later date.

When the aorta is controlled by a competent and well instructed assistant, the stage is set for removal of the embolus. The best plan, in these cases, is to select the most accessible spot on the anterior surface of the right common iliac artery. The adventitia is dissected off the anterior surface of the vessel over an area about 1 inch in diameter so that this structure will not interfere with the repair of the incision in the artery after the embolus has been removed. Through this area an incision 1.5 to 2 centimeters in length is made. In most cases, firm masses of thrombus or blood clot are encountered immediately. These begin to bulge through the incision. By the gentle compression of the vessel against the wall of the pelvis both above and below this incision, the clots are gently extruded. Those on the left side are swept through the left

common iliac vessel across the bifurcation of the aorta and downward to be extruded through the opening on the right side. When, on repetition of these maneuvers, no further clots are extruded and no other abnormalities can be left, the bulldog clamps are released for a few seconds and then reapplied, first on one external iliac artery and then on the other, then on each internal iliac artery. During each of these maneuvers, there should be active bleeding through the incision and, if the patient's blood pressure is good, the bleeding may show moderate pulsation, provided the circulation has been completely cleared of clots in all these directions. If these four points have shown satisfactory return-bleeding, the prospects are that a complete removal of obstructing masses had been accomplished. If such should be the case, a bulldog clamp is then applied to the left common iliac artery, near the bifurcation of the aorta and to the right common iliac 1 inch distal to the incision. When these have been adjusted nicely, the assistant controlling the aorta is directed to relax the pressure of the index finger on the aorta, momentarily. Occasionally further masses of clots are swept out through the incision with the force of the aortic blood pressure. If no further masses are present, free violent pulsating bleeding will occur. The squirt of blood from the incision should reach at least 6 feet from the operative field and in some cases it may fly as far as 15 feet. This is of considerable significance, indicating the freedom of the vessels, to this level, from further clots. An oozing or feeble bleeding from the incision indicates that further clots are present and must be removed.

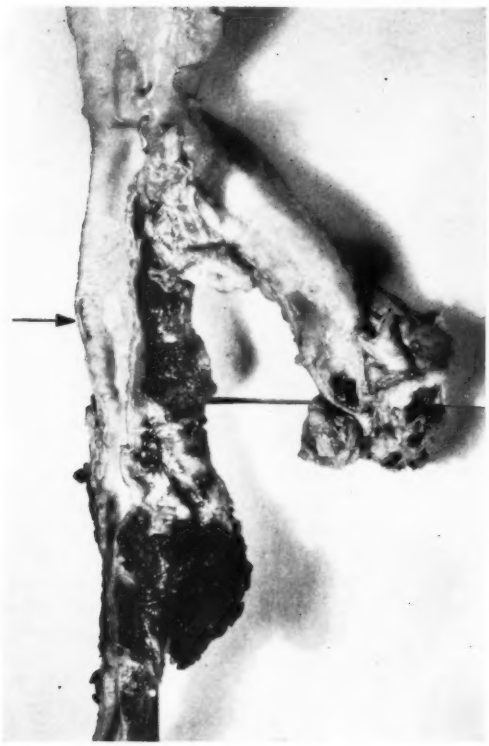
When by these tests it is proved that the circulation is cleared of clots, bull dog clamps are applied above and below the incision in the artery and 500 units of heparin in saline solution are placed in the lumen of the vessel through the open incision (3). With silk on a fine needle, the incision is then closed with a continuous suture. If the stitches are placed not more than 1/16 of an inch apart, there is usually no leaking whatever from the field. When the suturing has been completed, the bulldog clamps distal to the repair are removed first. At this time it is good practice to inject,

Fig. 2. Same field as shown in Figure 1. Arrow points to incision in right common iliac artery *b* through which the dark colored thrombus is being extruded.

obliquely through the wall of the right common iliac artery, about 800 more units of heparin in saline solution. Following this the aorta is released and the circulation returns through the vessels of the pelvis. If the operation has been satisfactory, normal distention and pulsation of all the vessels in the pelvis is obvious and, if there are no remaining masses in the circulation, observers at the feet can usually feel pulsation of the vessels at both ankles. The feet and legs change from a mottled cyanotic (5) or marble white hue, to a rosy pink color and the coldness is changed to one of warmth. If everything is satisfactory, the peritoneum is allowed to fall back and is sutured in the right iliac fossa. Any opening in the peritoneum in the region of the umbilicus is repaired and the abdominal wall is closed in layers without drainage.

If the operation has been completed satisfactorily, the results are most gratifying; the appearance of the shrunken extremities is changed from the pallor and cyanosis of impending gangrene to that of a normal rosy pink. The patient is returned to the ward, when continuous intravenous heparin is given in sufficient quantity to keep the blood clotting time at about 15 minutes for the following 3 days.

I. L. This patient, aged 19 years, had a history of chronic rheumatic myocarditis, mitral stenosis, auric-



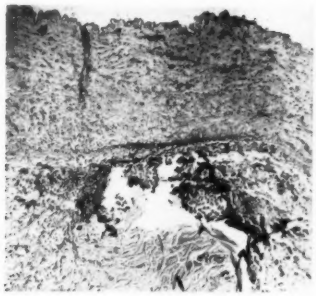


Fig. 3. a, left, Intima of aorta and common iliac arteries, showing healed incision at arrow 4 months following embolectomy. b, above, Showing healing of suture line.

ular fibrillation and insufficiency, dating from rheumatic fever in early childhood. The symptoms were sudden occlusion of the aorta with pain in sacral and hypogastric regions and extending down both legs to the toes. The feet were both white. The legs were mottled to the upper third of the thigh. There was cyanosis of the lower abdominal region. Both legs were cold to the upper third of the thighs. There was no pulsation in either femoral or other peripheral vessels. Anesthesia and paralysis were noted from the knees distally. There was marked myocardial failure and the patient was an extremely bad surgical risk.

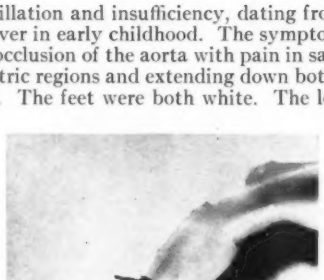


Fig. 4. Right common iliac artery showing healed incision following embolectomy.

Operation. Through a paramedian approach the iliac vessels and aorta were exposed. The embolus was demonstrated plugging the bifurcation of the aorta. It was manipulated into the right common iliac artery and removed through an incision in this artery. There was some doubt if all the clot had been removed from the left side. Following the operation there was normal pulsation in the right femoral and peripheral vessels and pulsation in the left femoral. The left popliteal and vessels in the feet did not have a normal return of pulsation, although the circulation to the extremity was adequate. There was no gangrene of feet or toes. The patient made an excellent recovery and was in relatively good health, apart from the disability from myocarditis, for a period of 2 years and 9 months. During this period the patient had many subsequent embolisms, having been admitted to hospital on four occasions with fur-

ther attacks of embolisms in mesenteric and peripheral vessels, the patient dying on the last admission with pulmonary embolism. At postmortem examination, sections of the iliac vessels showed occlusion of both common iliac vessels with organized thrombus. From the fact that the vessels were patent following the aortic embolectomy, it was assumed that subsequent attacks of embolism had caused occlusion of these vessels.

H. J. M., aged 64 years. November 22, 1941. Six days following an attack of coronary thrombosis the patient suddenly developed symptoms of complete aortic embolism. At operation the embolus was easily demonstrated at the bifurcation of the aorta. When the vessels were controlled the embolus was removed without difficulty, through a short incision in the right common iliac artery. Heparin treatment was started following this. The circulation returned normally to both feet. The femoral, popliteal, anterior and posterior arteries in both legs had normal pulsation and the feet had a normal color. The patient had recovered completely from the operation and was beginning to take food. Quite suddenly on the second day there was another severe attack of coronary occlusion from which she succumbed.

M. R., aged 38 years. Twenty-one hours before operation patient had an attack of lower abdominal and sacral pain extending down over both extremities. There was blotchy cyanosis of both legs extending over the lower abdomen on both sides. The legs were cold, anesthetic, and paralyzed. There was no pulsation in the vessels of the feet, popliteal space, or femoral arteries. This was a typical picture of complete aortic embolism of 21 hours' duration.

At operation the embolus occluding the aorta and both common iliac arteries was easily demonstrated. The thrombi from both sides were removed through an incision in the right common iliac artery. Seven hundred units of heparin were instilled into the lumen, and the incision was closed. Immediately following the operation the pulsation returned to anterior and posterior tibial vessels in both feet. The color turned to a rosy pink and the feet became warm. The sensation returned, but on the right side there was some impairment to touch and pain stimuli. The motor return was slower than the sensory but within a few days all muscle groups were acting fairly normally except for the anterior tibial group on the left side where there was some weakness lasting for about 1 month. The patient was able to walk and returned to normal health. Four months later the patient had a cerebral embolus from which she succumbed. At the postmortem examination the aortic and iliac vessels were clear of thrombi and the vessels were normal in every respect. The scar at the site at which the right common iliac artery was opened was healed with no signs of dilatation, thrombosis, or stenosis (Fig. 3).

M. L. S., aged 48 years. September 16, 1935. This patient had chronic rheumatic myocarditis with mitral stenosis and auricular fibrillation. She developed symptoms of aortic embolism with complete obstruction of arterial supply of both legs. At operation through the approach described, the aorta was demonstrated to be completely plugged and both common iliacs were also plugged. Through an incision in the right common iliac artery, after control of all peripheral vessels and aorta, the clots were removed completely. The patient made an uninterrupted recovery. The circulation became normal in both legs and there was normal pulsation in both femoral, both popliteal, and anterior and posterior tibial vessels in both feet. The patient was quite well following this episode, for 8 months. At this time the patient had another embolism in the right common femoral artery. This also was removed successfully. The patient made an uninterrupted recovery with normal circulation to the extremity. Again she was in quite good health until she died suddenly of cerebral embolism about 2 years following the original attack.

E. H., aged 27 years. This patient had chronic rheumatic myocarditis, mitral stenosis, and auricular fibrillation. There were four attacks of peripheral embolism. The first was in the left common femoral artery. It was removed by Dr. J. A. MacFarlane. There was normal return of circulation with pulsation at the periphery. Heparin was given for 8 days to prevent thrombosis following the operation. Nine days later the patient had an embolus in the right common femoral artery. This also was successfully removed followed by treatment with heparin for 3 days. Five days later the patient had symptoms of aortic embolism. This was successfully removed and treatment with heparin was given for a few days. About 3 weeks later the patient had symptoms of a small cerebral embolism from which she recovered without disability. Since that time there have been no further embolisms and the patient is in quite good health with very little disability now 3 years and 6 months later. There are no signs of cardiac failure. She is so well that she is able to skate and take active part in sports.

O. J. The patient had rheumatic myocarditis with mitral stenosis and auricular fibrillation. Thirty-three hours before the time of operation the patient suddenly developed symptoms and signs of complete obstruction of bifurcation of the aorta. At operation an embolus was demonstrated occluding the aorta and both common iliac arteries. These were removed through a short incision in the right common iliac artery. Heparin treatment was started. Immediately following the operation there was normal pulsation in the femoral, popliteal, anterior and posterior tibial vessels in both feet. The patient had recovered satisfactorily from the operation, but on the second day the patient suddenly had symptoms of a massive cerebral embolism from which she died within a few minutes.

CONCLUSIONS

1. Embolism of the aorta is treated satisfactorily by surgical removal.

2. An extraperitoneal abdominal approach gives a satisfactory exposure through which the operation can be carried out without difficulty.

3. In spite of the fact that most of these cases eventually die of embolism, the patient can be completely relieved of symptoms and return to the original state of health, following surgical treatment of the immediate episode.

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PREVENTION OF GANGRENE FOLLOWING LIGATION OF MAJOR ARTERIES—EXPERIMENTAL STUDY

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GANGRENE of the lower extremities is a frequent consequence of aortic embolism at the bifurcation or after trauma to the major arteries of the lower extremities (2, 7, 10, 12, 13, 15–17). Since the vascular bed peripheral to the site of interruption of the circulation is patent for a varying time—6 hours to a week or more—after occlusion, it appeared to us that delivery of a nutrient fluid into the arteries distal to the obstruction might be feasible. Such a procedure might maintain the viability of the extremities, permitting a more favorable outcome, such as canalization of the embolus with partial return of the circulation or development of collateral circulation (1).

We approached this problem experimentally in animals. It became necessary to develop a reliable technique for producing gangrene of the lower extremities, after which the effect of infusing nutrient material into the arteries could be evaluated.

Production of gangrene. Some difficulty was encountered in determining the proper arteries to be ligated in order to produce gangrene consistently. Simple ligation of the aorta at the trifurcation was a remarkably innocuous procedure in cats. They showed no restriction of muscular activity even on the first day after operation. Bilateral ligation of the femoral arteries, of the common iliacs, and of both the aorta and the common iliacs failed to produce gangrene.

Only when the anastomotic branches of the deep femoral arteries were ligated in addition to the large terminal branches of the aorta; or when the aorta, common iliacs, and midhemorrhoidal arteries were ligated, did *bilateral* gangrene result. As shown in Table I, 10 of 12 cats developed paralysis of both lower extremities within 12 hours, and massive gangrene in 1 to 2 weeks.

We next attempted to produce *unilateral* gangrene in cats. Ligation of the middle hemorrhoidal, common iliac and corresponding femoral anastomotic branches resulted in unilateral paralysis followed by gangrene in 4 of 5 such experiments. This appeared later than when bilateral ligations were performed.

Some control studies were also made in dogs, but these were not as numerous or as varied as in the cats. In 3 consecutive experiments, in which only the 3 terminal branches of the aorta were ligated, gangrene did not occur; in the next 3 consecutive experiments, with the same technique, gangrene did develop in 2 to 5 days.

To summarize this phase of the problem—a reliable technique for producing gangrene of the lower extremities in cats, both bilaterally and unilaterally, was developed.

From the Laboratories of The Mount Sinai Hospital.
Dr. Milton Mendlowitz aided in this study with valuable technical assistance.

Delivery of nutrient fluid. We then studied the delivery of nutrient fluid into the femoral artery distal to the ligation. We had observed that in the gangrenous extremity of the cat, the femoral artery is patent up to a week after operation. When cut below the level of ligation, it oozes blood, and fluid can be forced into it by hand with a syringe. Either the heart's force or a substitute pulsatile pressure is required to overcome the peripheral resistance of the arteriolar-capillary portion of the circulation.

Physiological amounts of fluid to be circulated. The blood volume of the cat is about 100 cubic centimeters, and the normal blood flow through the cat's femoral artery is 50 cubic centimeters per minute. The continuous addition of extrinsic fluid in the amounts needed for maintenance of viability of the extremity produces an unphysiological increase of blood volume, resulting in anasarca and death.

To avoid this increase in blood volume, we attempted to use the animal's own blood for delivery into the recipient artery distal to the ligation. We found the cat unsuitable for this series of experiments and transferred our studies to dogs, in whom the technical difficulties were not so great.

Recirculation experiments. We recirculated the animal's blood from a donor vessel to the recipient femoral artery in two types of experiments: (1) A *donor artery* was connected directly to the femoral artery utilizing the heart action to transmit the blood from the former to the latter; (2) blood was aspirated from a *donor vein* by means of a machine which then forced it into the recipient femoral artery, imitating the pulsatile pressure of the cardiac action.

The details of both types of experiments will be discussed.

Anticoagulants. The problem of anticoagulants of course became important in the work on extracorporeal blood flow. Various anticoagulants were tried.

1. Cystein hydrochloride was useless in all doses (14).

2. Dicoumarin was given by mouth for 2 days before operation. Though the coagulation time was increased to 45 minutes, a soft clot formed in the tubing in about 15 minutes.

TABLE I.—LIGATION EXPERIMENTS IN CATS

	No. of animals
A. No paralysis or gangrene—	
Femoral arteries	2
Aorta just above trifurcation (1 paralyzed; no gangrene; died 2 days)	4
Common iliac arteries	2
Aorta and internal iliacs (1 paralyzed only on right side)	1
B. Bilateral paralysis and gangrene—	
All branches of aorta at the bifurcation or trifurcation and of the deep femoral arteries of both sides	–
All branches of aorta and external iliac or femoral arteries	10 of 12
Aorta, common iliac and midhemorrhoidal arteries	2
C. Unilateral paralysis and gangrene—	
Middle hemorrhoidal, common iliac and corresponding femoral profunda arteries	4 of 5

3. Chlorazol B pink (11), in doses of 100 milligrams per kilogram intravenously, was effective and had no toxic action. The substance stains the tissues a brilliant cerise for weeks. The blood tested immediately after injection of the dye is incoaguable. At the end of 6 hours the coagulation time was 15 minutes. It was necessary to give injections of half the initial dose about every 4 hours.

4. Heparin was the most satisfactory, but because of its expense was used only in crucial experiments. It was used both in divided doses and as a continuous intravenous infusion diluted with normal saline.

Artery-to-artery. Nembutal anesthesia was used.

1. In a cat prepared with chlorazol B pink, both femoral arteries were ligated. By means of cannulas and glass-and-rubber tubing one femoral artery *proximal* to its ligation (donor) was connected to the opposite femoral artery *distal* to its ligation (recipient). A pulsation in the recipient artery was present for 2 hours, after which time the movement of the cat kinked the tubing and the blood clotted in the cannulas.

2. A similar experiment in a dog resulted in pulsation in the recipient artery for 5 hours before clotting occurred.

3. Attempts to anastomose one partly freed femoral artery to the recipient femoral artery by means of cannulas *around* the arteries were

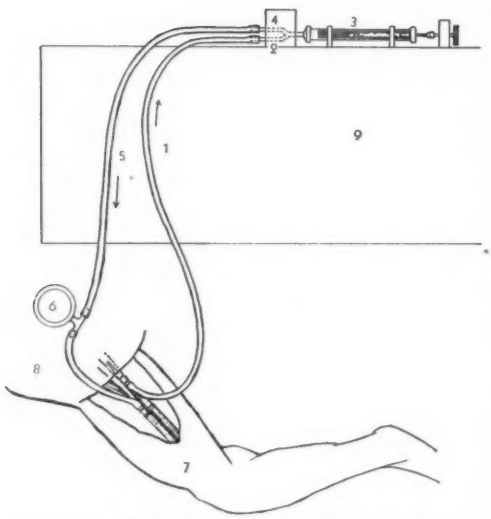

Diagram of vein-machine-artery sequence. *1*, Cannula and rubber tubing in the femoral vein, with cannula directed *centrally*; *2*, portion of 2 way valve leading to syringe, *3*, of pipetting machine, 1 cubic centimeter, with adjustable stroke; *4*, portion of 2 way valve leading from syringe, *3*; *5*, rubber tubing leading from 2 way valve to femoral artery, with cannula directed *distally*, beyond site of ligation; *6*, aneroid blood pressure gauge; *7*, right lower extremity of dog; *8*, abdomen; *9*, case enclosing motor for pipetting machine.

unsuccessful in the cat, principally because of the small caliber of the vessels.

4. In a dog prepared with chlorazol B pink, the femoral artery was ligated and a 3 inch segment of femoral and external iliac artery proximal to the ligation was dissected free. The numerous small branches were doubly ligated and divided. The stripped vessel was drawn subcutaneously through the lower abdominal wall to reach the recipient femoral artery of the opposite side. Donor and recipient arteries were joined by a cannula. The transmitted pulse was present in the recipient artery for 10 hours. The cannula became blocked in 24 hours and the experiment was terminated. The dog died in 2 days. Dissection of the artery and ligation of the minute branches was an extremely time-consuming and shocking procedure.

5. For clinical purposes it would be necessary to use an artery in the upper extremity as donor. Therefore, the axillary and the homolateral femoral arteries of a dog were exposed and ligated. The axillary artery was the donor for the recipient femoral artery. The vessels were connected by means of cannulas and glass-and-rubber tubing. A pulse was obtained in the rubber tubing and in the recipient artery for 8 hours. Because of an overdose of nembutal the animal's respiration slowed, the blood as seen in the glass tubing became cyanotic, and the pulse was rapid and faint. The experiment was terminated because of the animal's condition and because of clotting, in about 12 hours.

6. The same operative procedure was performed on a dog in whom heparin was the anticoagulant. The animal was given divided doses of heparin so that the coagulation time was between 5 and 45 minutes. The nembutal anesthesia was light. After recovery from the nembutal, the animal was maintained in light sleep by means of small doses of morphine sulfate given subcutaneously about every hour. The general condition remained excellent.

The tubing was cleaned several times to remove soft clots. The color of the shunted blood was bright red. Blood flow was maintained for 11 hours, and a pulse was palpable in the rubber tubing and in the femoral artery below the ligature.

Vein-to-artery. In order to deliver blood from a vein, with its negative pressure, to the artery with its positive peripheral resistance, we used a pipetting machine, designed by the late Dr. Louis Gross, which is operated electrically and is capable of running continuously for 2 weeks.

The machine consists of a syringe with a two-way valve and attachments of tubing for alternate aspiration and expulsion of fluid. By varying the caliber of the syringes and the set of the plunger, .001 cubic centimeter to 2 cubic centimeters may be delivered per stroke. The machine can work against a resistance of 50 pounds. An aneroid gauge in circuit with both the machine and the animal indicated the pressure in millimeters produced by the machine. In some experiments, a closed mercury manometer was used instead. This pressure is not under the experimenter's direct control, as the machine actually produces only

that pressure which is necessary to overcome the peripheral resistance in the vascular bed. The normal pressure in cats and dogs is about 130 millimeters of mercury. When the animal is in shock or when there is a leak in the circuit, the pressure falls below this level; when there is partial obstruction in the outflow tubing or cannula the pressure readings climb.

7. We attempted to aspirate blood from the femoral vein, directing the cannula distally. After a few minutes, no blood could be obtained and the lumen of the vein collapsed under the aspirating force of the pump.

8. In mammals, the abdominal veins and the innominate vein form a venous reservoir. In man, it contains about 400 cubic centimeters of blood and communicates with the portal-hepatic reservoir, which contains 1000 cubic centimeters (8).

This venous reservoir was used as the source of blood for the recipient artery. This was done by directing the cannula *centrally* in the femoral vein, passing it under Poupart's ligament into the external iliac vein.

It was estimated that about a fourth of the usual blood flow to the lower extremity is necessary for maintenance of basal nutrition. In a 20 to 25 kilogram dog, the blood flow through the femoral artery is 90 to 100 cubic centimeters per minute. We estimated the blood flow in smaller dogs. The pipetting machine was set to aspirate one-quarter of the normal blood flow per minute from the venous reservoir. The blood was pumped into the contiguous femoral artery. This was done for as long as 2 hours. The details of several of these experiments are indicated in Table II.

In several of the animals there was difficulty in aspirating amounts greater than the calculated minimal requirement. More of these experiments are necessary to determine, and if possible to eliminate, the reason for the variation in the quantity which could be aspirated. For any long term experiments in recirculation of venous blood, a method of oxygenation is necessary.

TABLE II.—AUTOTRANSFUSION FROM EXTERNAL ILIAC VEIN TO LIGATED FEMORAL ARTERY IN DOGS

No. of dog	Weight—kgm.	Cubic centimeters per minute aspirated by machine	Duration of flow
374	13*	15, right extremity 15, left extremity	2½ hrs. ½ hr.
402	19	30	2 hrs.
286	18	15 (30, not successful)	2 hrs.
327	12.2	18 (30, vein collapsed)	2 hrs.
453	22	60	45 mins.

*3 wks. later.

ANALYSIS OF STUDY

We attempted to devise a means of preventing gangrene of the lower extremities in cats and dogs whose arteries had been ligated, in order to apply it to man. Contrary to the reports of previous work (3) we had many failures before we finally developed a method by which paralysis and gangrene of the lower extremities could be produced. Numerous experiments were done in an attempt to transfuse blood from a donor artery or vein to a femoral artery distal to the site of ligation. Enough of these experiments were successful to prove the feasibility of this procedure, though many technical details remain to be worked out.

The simplest method is the autotransfusion from a donor artery of an uninvolved extremity. This requires only the use of an anticoagulant and a connecting tube. The objection which might be raised to this procedure in man, is the possible sacrifice of an important artery in a normal extremity. Experiments should be done to determine the suitability of *small* arteries as donor vessels, the loss of which would be of no serious consequence (4, 9).

To meet the objection of using an artery as the donor vessel, veins were used as the source, by aspirating with the pipetting machine and delivering the venous blood into the artery. The amount of blood obtained from the distal portion of the femoral vein is inadequate for continued delivery. The large abdominal venous reservoir was aspirated through the *central* portion of the femoral vein and was found to be a satisfactory source.

This method presents two additional problems: first, oxygenation of the venous blood. Gibbon most recently has worked extensively

on the problem of extracorporeal oxygenation of venous blood, but his method has not been applicable to our apparatus. The second problem is: How much blood should be delivered to maintain the viability of the extremity? As a clinical observation in patients with peripheral vascular disease, we know that a fraction, perhaps one-quarter, of the normal arterial blood supply is all that is essential for the preservation of an extremity. By analogy, it should be possible to maintain the viability of an extremity following an acute arterial closure by a similarly reduced amount of blood. Our experiments showed that it is possible to obtain such an estimated quantity from the abdominal venous reservoir.

While the experiments described are suggestive, they are not sufficient to prove unquestionably the value of the methods. When all the technical problems have been solved, the method must be applied in crucial long term experiments in animals, before its use can be recommended in human beings.

SUMMARY

1. Bilateral ischemic paralysis and gangrene of the lower extremities in cats was produced in 10 of 12 experiments in which the 3 terminal branches of the abdominal aorta and the anastomotic branches of the femoral arteries were ligated.

2. Unilateral ischemic paralysis and gangrene of the lower extremity was produced in cats in 4 of 5 experiments in which the middle hemorrhoidal, the common iliac, and the homolateral anastomotic branches of the femoral artery were ligated.

3. In 3 of 6 experiments on dogs, gangrene of the lower extremities was produced by ligating the three terminal branches of the aorta.

4. The blood supply to the lower extremity after ligation of the common iliac artery, was maintained for several hours by autotransfusion. In some experiments the blood was transfused from *donor arteries*. In other experiments blood was aspirated from the abdominal *venous reservoir* and pumped into the femoral artery by a pipetting machine.

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THE USE OF AUTOTRANSFUSION IN SURGERY OF THE SEROUS CAVITIES

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EMERGENCY surgery of the serous cavities of the body, particularly in the field of trauma and of ruptured ectopic pregnancy, is directed principally to the control of hemorrhage and the replacement of blood in an often exsanguinated patient. The time factor is extremely important. This is true, not only in regard to hemostasis, but also in the replacement of blood when large amounts have been lost rapidly. It is obvious that the prevention of shock due to hemorrhage by rapid replacement therapy is to be preferred to the frequent custom of instituting therapy only after shock has become evident. Even after shock is present, the earlier it is controlled the less likelihood there is of irreversible changes.

Hamilton in a review of 336 cases of penetrating wounds of the abdomen found that hemorrhage was the greatest factor in the mortality. In his series there was a mortality of 27.8 per cent in cases of hemorrhage of less than 500 cubic centimeters, 51.3 per cent in those between 500 and 1000 cubic centimeters and 73.4 per cent in those with over 1000 cubic centimeters. This has been borne out by others: Billings and Walking, Loria, Rippy, Taylor, and Mason.

While wounds in the superficial portion of the lungs are usually not dangerous from the standpoint of hemorrhage, there is a definite group of thoracic wounds in which exsanguination may occur. Griswold and Maguire state:

"When massive cardiac hemorrhage into the pleura is occurring the exact diagnosis of wound of the heart may be more difficult, but the indications for immediate operative intervention are clear and imperative. Bleeding from the parenchyma of the lung in wounds of the thorax may be massive, but is slow and seldom requires operative hemostasis. On the other hand, free bleeding from the heart, great vessels, internal mammary, or intercostal arteries is fast and profuse. Rapidly progressive shock is present early and death may quickly ensue unless hemorrhage is checked."

Elkin advises immediate operation when there is evidence of rapidly increasing hemorrhage, or a wound of the heart. In his series of patients with thoracic wounds, the most common cause of death was shock and hemorrhage. He states:

"Treatment of this class of patients presents the most difficult problem and 18 of them died within the first 24 hours after admission without reacting from shock. Some of that number may have been saved by operation. This would have necessitated open thoracotomy and lung suture."

We believe that in certain cases of this type, aspiration of blood from the thorax, replacement by air, and reinfusion of the blood may be lifesaving without subjecting the patient to risk of open thoracotomy and lung suture.

Likewise, in ruptured ectopic gestation the principal cause of death is from exsanguinating hemorrhage.

A review of such cases by any surgeon will show that an outstanding proportion die on the operation table or shortly after operation, due to tardy or inadequate replacement of the lost circulating blood volume. The time lost in grouping donors, matching blood from a bank, or even obtaining plasma in sufficient amounts may be fatal. Also, the amount of blood of correct type and of plasma available from donors, blood banks, etc., frequently is insufficient to supply the needs of patients who have lost large amounts of blood (1500 to 2500 c.c.). The usual 500 cubic centimeter transfusion is the donor's dose and bears no relationship to the needs of the patient.

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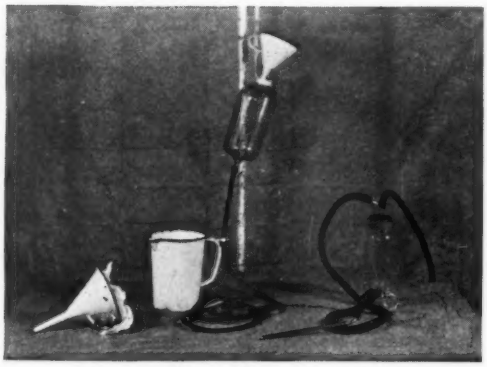

e d f a b c

Fig. 1. Autotransfusion outfit used in all cases of hemorrhage into body cavities: a, Pool suction tip; b, 500 cubic centimeter bottle with two-hole stopper containing citrate solution; c, tube running to operating room suction; d, 1000 cubic centimeter graduate; e, funnel with gauze filter; f, intravenous outfit with Murphy drip.

All too often one sees several pints of blood thrown away from the body cavity of patients who are bleeding to death. It is our belief that this autogenous blood represents the most readily available, abundant, rapid and safe replacement therapy for these urgent cases. Large quantities of blood are often immediately accessible, the blood is compatible and needs no crossmatching, the danger of transmission of disease, i.e., syphilis, malaria, etc., is absent, as is the possibility of an allergic response.

In 1874 it occurred to William Highmore, after seeing a patient exsanguinate from postpartum hemorrhage, that had he collected, defibrinated, and reinfused the blood, it would have offered the woman her only chance of life.

The first reference to the actual infusion of autogenous blood was made by John Duncan in 1885. He was faced with the problem of thigh amputation on a patient whose leg had been crushed, and who had become moribund during transportation to the hospital. Donors were not immediately available, so during the amputation approximately 3 ounces of blood which fell were collected in a dish containing phosphate of soda. This was then reinfused into the femoral vein on the amputation stump. The case terminating successfully, the procedure was repeated in other instances, and he stated:

"I am convinced that this little operation, so easily performed will save many lives in the collapse of primary amputations and will prove beneficial to the wasted and anemic patients in the major amputations for disease."

The first report of autotransfusion of blood collected from the peritoneal cavity was given by Theis in 1914. In the cases he reported, ruptured ectopic pregnancy was the cause of hemorrhage. In 1936, Watson and Watson in a review of the American literature reported 275 cases and added 2 of their own. The largest individual series was that of L. J. Tiber, who had used the procedure in 189 cases of ruptured ectopic pregnancies.

In spite of these reports, the autotransfusion has never enjoyed widespread popularity. Too frequently it has been unjustifiably condemned and the use of it neglected when it would have been of utmost value in the restoration of blood volume. This attitude has been derived from reports of bad results, which we believe were due not to the method, but to errors in its use.

In this report, 100 consecutive autotransfusions have been analyzed. The first of these were done in cases of intraperitoneal hemorrhage due to ruptured ectopic pregnancy, but later the transfusion of autogenous blood was used in a large variety of emergency cases with internal bleeding.

Table I shows the type and number of cases in which autotransfusion has been used. The marked increase in cases since 1937 was due to increased emphasis on the procedure and the use of blood in cases of hollow viscus perforation. Also, at this time, a suction apparatus was devised to collect the blood. The apparatus is very simple (Fig.1) but serves the purpose well and is easily sterilized and placed upon the instrument table. The unit consists of a 500 cubic centimeter graduated flask fitted with a rubber two-hole stopper and glass connecting tubes. Before the operation is begun 50 cubic centimeters of 2 per cent sodium citrate solution is placed into the flask. One tube is then attached to the suction and the other to the Pool suction tip. When in use, the flask acts as a trap, collecting the blood.

TABLE I.—TYPE AND NUMBER OF CASES RECEIVING AUTOTRANSFUSIONS

Type	Year										Total
	1933	1934	1935	1936	1937	1938	1939	1940	1941	1942*	
Ruptured ectopic pregnancies	2		1		4	3	2	4	5	1	22
Penetrating wounds of the thorax without involving the pericardium				1			3		1		5
Penetrating wounds of the thorax involving the pericardium and heart					2	3		2	5	2	14
Nonpenetrating wounds of the abdomen		1	2		1	1	2	1	9	4	21
Penetrating wounds of the abdomen without perforation of a hollow viscus		1			2	1		2	7	1	14
Penetrating wound of the abdomen with perforation of a hollow viscus					1	7	1	7	7	1	24
Total	2	2	3	1	10	15	8	16	34	9	100

*1942 includes only January and February.

Two flasks are kept sterile so that as soon as one becomes filled the other may be put in its place. After the blood is collected in this manner it is filtered through 10 thicknesses of gauze into a graduated cup and then refiltered into an intravenous set from which the patient is receiving 0.85 per cent saline solution. By using the two flasks interchangeably, a large quantity of blood may be collected and returned to the patient without delay.

Cordovil (4), Wallingford, Willis, and others have described similar techniques for the collection and reinfusion of blood. The use of suction is superior to either mopping or ladling the blood. Not only is time saved but regions difficult to reach with a sponge or ladle are made easily accessible by the use of the Pool suction tip and almost 100 per cent recovery of the blood is possible. Loss and spillage are minimized by introducing the tip into the body cavity before the entire incision has been made. The degree of hemolysis due to injury of the erythrocytes is not so great when the blood is collected by suction as it is when squeezed from a sponge.

In experiments by Filatov, he found that after a single filtration through 2 to 4 thicknesses of gauze, small clots and fibrin flocculation were present in the filtrate but these were absent after filtration through 8 thicknesses. He further said that the use of filter paper was the best, but because of slowness was not practical. In the technique described, the blood is filtered either 1 or 2 times through approximately 10 thicknesses of gauze and this has proved satisfactory. Improper filtration may be serious and was the cause of the only death, in our series, which could be directly attributed to the autotransfusion.

In the 100 cases reported in this series the amount of blood reinfused varied widely. The smallest volume returned was 200 cubic centimeters and the largest amount 2500 cubic centimeters. In 8 cases the amount was not stated, while in the remaining 92 cases the average blood return was 950 cubic centimeters each, the mean volume between 500 and 1000 cubic centimeters (Table II).

The volume of blood returned in this series compares very closely to the 67 cases reported by Cordovil (5) and is greater than the amount per case returned in Filatov's series. The latter, however, ladled the blood from the body cavity, and this may account for the smaller quantities.

When such large volumes of blood may rapidly be returned to patients in shock due to internal hemorrhage, one may readily appreciate how the procedure may frequently be lifesaving, as well as being beneficial in the convalescence of those patients with a lesser degree of anemia.

In the 100 patients in this study, 67 were in shock and in 5 there were signs of impending shock. In 11 others the systolic blood pressure was below 100 millimeters of mercury but no other signs of shock were recorded while in 17, signs of vascular collapse were not present in the preoperative period.

TABLE II.—AMOUNT OF AUTOTRANSFUSIONS

Amount of blood—c.c.	No. Cases
Less than 250	2
250 to 500	13
500 to 750	26
750 to 1000	16
1000 to 1500	12
1500 to 2000	15
2000 to 2500	8
Not recorded	8

Disadvantages and contraindications to the use of autotransfusion have been given in the literature, and reactions ranging in severity, from mild increase in temperature, or nausea and vomiting, to fatalities, have been reported.

The causes usually given for reaction are: (1) toxins or foreign protein coming from necrotic or decomposing tissue which may be in the body cavity during or following the hemorrhage, i.e., the gestation products of a tubal pregnancy or crushed liver tissue in cases of trauma; (2) bile mixed with the blood in injuries to the liver; (3) the use of portal blood before it has gone through the liver; (4) bacterial contamination from penetration of a hollow viscus; (5) hemolytic changes of the blood.

Toxins or foreign proteins caused by necrosis of tissue. In 22 cases of ruptured ectopic pregnancies reported in this series there were no deaths and only 1 reaction. The type reaction was not stated, only that it was mild. In this case the patient had been admitted 6 days prior to operation with a provisional diagnosis of ruptured ectopic gestation. At operation 1500 cubic centimeters of dark unclotted blood was found in the peritoneal cavity. The reaction caused by the infusion of this blood was probably due to hemolysis and will be discussed under that heading.

In Tiber's (24) series of 189 cases of ruptured ectopic pregnancies which received autotransfusion, 123 patients received this alone, while in the remaining 66 patients the autogenous blood was supplemented by transfusion from donor sources. In the former cases the mortality was 0.81 per cent, while in the latter it was 3.03 per cent. Three fatalities were reported with the cause of death as blood dyscrasia, and in all 3 operation was done after 72 hours. The term, blood dyscrasia, is very vague and it must be assumed, because of experimental work from other sources (12, 19) on blood allowed to remain in a serous cavity, that it was a hemolytic reaction. Since the publication of his report, Tiber has used the autotransfusion in 250 more cases, in none of which was there a reaction (25).

Trimble (16), in discussing a case reported by Allen, in which 800 cubic centimeters of blood from the peritoneal cavity was reinfused in a patient with a ruptured liver, and who died 56 hours later, stated that the cause may have been due to damage done by toxins elaborated by a ruptured liver in which autolysis takes place so rapidly.

The 24 cases of liver injury in this series are presented in Table III. In this group there were 9 fatalities, 3 occurring on the operation table and 5 within the first 3 postoperative days. The remaining 1 had an associated injury to the right kidney which necessitated nephrectomy. Autopsy following death on the 19th day showed the remaining kidney to be almost totally replaced by a solitary cyst. In all of the fatal cases there were severe associated injuries and in no instance was death believed due to the reinfused blood. In the 15 cases which survived there were no reactions. In 2 of these, large masses of tissue were torn from the liver. In wounds of the spleen where there was crushed splenic tissue and blood was reinfused, there was likewise no reaction.

Bile mixed with the blood and injuries to the liver. The belief that bile is toxic when present in the blood and in sufficient quantities fatal has been confirmed experimentally (30). When bile is injected into the blood stream it has a depressing effect on the central nervous system and heart muscle from its direct action on these organs, and destroys the red blood cells, as do saponins, by reducing the surface tension (6).

Undoubtedly, in injuries of the liver there are varying amounts of bile mixed with blood in the peritoneal cavity. The most important factors in the amount of bile which escapes from the liver, are the type of injury and the time between injury and operation. In stab wounds the amount of bile liberated is probably minimum, while in crushing wounds or fractures of the liver, a much larger quantity is free and mixed with the blood. However, in

TABLE III.—CASES WITH INJURY TO THE LIVER

Cases	Type of injury	Autotransfusion in		Remarks
Associated injuries		c.c.*	Result	
1 +	N.P.	2000	D	Died 2d postoperative day. Associated injuries—ruptured spleen and fractured femur
2 +	N.P.	1500	I	250 gram mass of liver tissue free in peritoneal cavity. Associated injuries—ruptured kidney and fractured radius
3 +	N.P.	700	I	Associated injury—fractured skull
4 o	N.P.	2000	D	Died 3d postoperative day. Severe injury to liver with 5 by 8 cm. piece of liver free in peritoneal cavity. Autopsy revealed necrosis of the liver and 1000 c.c. of blood in the peritoneal cavity
5 o	N.P.	1500	I	
6 +	N.P.	1000	I	Associated injury—concussion of the brain
7 o	N.P.	800	I	
8 o	G.S.W.	350	I	6 by 3 cm. piece of liver tissue floating free in the peritoneal cavity
9 o	S.W.	700	I	
10 +	G.S.W.	1000	D	Died day of admission. Autopsy revealed penetration of chest, left lung, diaphragm, stomach, and liver. Also gunshot wounds of mouth, penis, and perineum. Massive hemothorax
11 +	G.S.W.	1500	D	Died during operation. Large perforation of inferior vena cava
12 +	G.S.W.	800	I	Associated injuries—crushing wound of spleen, perforation of stomach with gastric contents in peritoneal cavity
13 +	G.S.W.	750	I	Associated injury—hematoma around kidney
14 +	G.S.W.	400	I	Associated injuries—perforation of stomach, and penetration of kidney necessitating nephrectomy
15 o	S.W.	500	I	
16 +	G.S.W.	2000	D	Died on 2d postoperative day. Autopsy revealed rupture of accessory splenic vein, ruptured kidney and pancreas, perforation of stomach and jejunum
17 +	G.S.W.	2500	D	Died during operation—perforation of aorta
18 +	G.S.W.	1200	D	Died during operation—perforation of inferior vena cava, kidney, and small bowel
19 +	G.S.W.	900	I	Two perforations of stomach
20 o	S.W.	300	I	
21 o	G.S.W.	300	I	
22 +	G.S.W.	700	D	Right nephrectomy because of severe injury to right kidney. Patient died of uremia 19th postoperative day and autopsy revealed left kidney replaced by a solitary cyst
23 o	G.S.W.	700	I	
24 +	G.S.W.	800	D	Died 2d postoperative day. Associated injuries—rupture of spleen and perforation of diaphragm

N.P.=Nonpenetrating wound.
G.S.W.=Gunshot wound.
S.W.=Stab wound.

*Cases 4 and 16 died following transfusions; no reaction in other cases.
I. Improved; D, died.

the 7 nonpenetrating wounds which were crushing in nature, there were no hemolytic reactions or any evidence of depression of heart action.

In Case 8 (Table III) a 6 by 3 centimeter piece of liver was torn from the left lobe by gunshot wound. This mass was floating free in the peritoneal cavity. It was removed and

350 cubic centimeters of blood was reinfused. No reaction followed this and the patient had an uneventful recovery. The temperature rose to 102.6 degrees and the pulse was 104 per minute on the 5th postoperative day and returned to normal on the 8th postoperative day, remaining so throughout the hospital course. Also in Case 2 (Table III) a 250 gram mass of liver tissue was avulsed from the right lobe, being attached only by a thin pedicle, and the gall bladder was torn from its bed, being attached by the cystic duct. In this case the liver pedicle was divided and the free mass of liver tissue removed as well as the gall bladder. Nephrectomy was done for an associated fragmentation of the right kidney. This patient received 1500 cubic centimeters of blood from the peritoneal cavity. Recovery was uneventful, the temperature never exceeded 101.2 degrees, and there was no bradycardia or abnormality of the pulse rate. On the 9th postoperative day the temperature was normal and the patient was discharged improved on the 20th day.

Although aware of the toxicity of bile in the blood, injuries to the liver have not been a contraindication to autotransfusion on our service, and no serious reactions have taken place.

The use of portal blood before it has gone through the liver. The hemoclastic crisis, caused by injecting blood from the portal system into the systemic circulation as described by Widal, was not found present by Filatov in his experiments on autotransfusions in dogs and he concluded that the use of portal blood was harmless. Likewise, in the cases of this series in which the hemorrhage or a portion of it was from the portal circulation, there was no such reaction found.

Bacterial contamination from penetration of a hollow viscus. There are but two reports in the literature in which blood from the peritoneal cavity was reinfused following the perforation of a hollow viscus. The case of Wolf had a fatal termination following the use of blood from the peritoneal cavity in which there were perforations of the stomach and injury to the liver. Von Schaick, in 1927, reported the use of and recommended autotransfusion as a lifesaving procedure in penetrating wounds of the abdomen, with or without hollow viscus penetration.

Bacterial contamination of the blood due to perforation of a hollow viscus has been one of the major contraindications to the use of autotransfusion. It has been the opinion that by the use of such blood, septicemia and septic emboli would be the natural sequelae, seriously complicating an already unhappy situation. We have not found this to be true. A temporary bacteriemia does occur when contaminated blood is infused, just as it does when organisms are freed into the peritoneal cavity, but the blood stream destroys the bacteria without resulting infection.

Experimental evidence with normal animals has shown that there is a rapid passage of bacteria from the peritoneal cavity, via the diaphragmatic lymphatics, into the blood stream. Subsequent studies of the fate of the bacteria revealed that they were cleared relatively rapidly from the blood stream, and, after their disappearance, viable bacteria could still be isolated from the liver and spleen (26).

The cases in this series cannot be classified as normal because of the acute anemia resulting in a lowered resistance, and it is realized that by the infusion of contaminated blood a greater number of bacteria is placed into the circulation. However, by replacement of the blood and maintenance of adequate circulation, the resistance of the host more than compensates for the added number of bacteria. Should the virulence of the organisms be so great that the blood stream is unable to cope with them and a fatal septicemia occur, the same termination would probably result from the migration of the bacteria through the lymphatics, or death would occur from an overwhelming intraperitoneal infection.

If a sufficient quantity of sterile compatible blood is immediately available, its use would be safer than the use of contaminated blood. In such an instance the resistance of the host is increased without an increase in the number of organisms, while both are increased when contaminated blood is used.

In 1937, for the first time on the surgical service of the Louisville City Hospital, blood from the peritoneal cavity that had been

TABLE IV.—CASES WITH PERFORATIONS OF A HOLLOW VISCUS

Cases Associated injuries	Type of injury	Hollow viscus penetrated	Autotransfusion in		Remarks
			c.c.*	Result	
1 o	N.P.	Ileum	500	I	Two severe reactions during postoperative course from transfusions of blood taken from Blood Bank
2 +	G.S.W.	Stomach	700	I	Bullet traversed left pleural cavity and empyema later developed on this side
3 +	G.S.W.	Stomach	1000	D	Died 4 hours after operation. Autopsy revealed penetration left lung, diaphragm, stomach and liver. Also gunshot wounds of mouth, penis, and perineum. Massive hemothorax
4 +	G.S.W.	Colon	400	I	Perforation of the entire wall of the colon (questionable)
5 o	G.S.W.	Small bowel, tr. colon, descending colon	?	D	Died on 84th postoperative day. During postoperative period developed peritonitis and subphrenic abscess. The latter was drained on two occasions and the abdomen re-explored on one occasion
6 +	G.S.W.	Gall bladder	1500	D	Died during operation. Large perforation of inferior vena cava
7 +	G.S.W.	Stomach	800	I	Penetration of pleural cavity and injury to spleen with splenectomy
8 +	G.S.W.	Stomach	935	D	Died several hrs. after operation—autopsy revealed massive hemothorax with exsanguination. Also only one of two perforations of the stomach had been closed
9 +	G.S.W.	Jejunum, tr. colon	700	D	Died a few minutes after operation. Great difficulty in controlling retroperitoneal hemorrhage during operation
10 +	G.S.W.	Small bowel	600	D	Died during operation
11 +	G.S.W.	Duodenum, ileum, tr. colon	?	D	Died 17 hrs. after operation. Loop of ileum resected because of severe damage it sustained. Also perforation of the inferior vena cava
12 o	G.S.W.	Stomach, tr. colon	750	D	Died 13 hrs. after operation. Obstructive resection because of severe injury to colon
13 +	G.S.W.	Stomach	400	I	Associated injuries to kidney and liver
14 o	G.S.W.	Small bowel	1300	D	Died day of operation. Pulse and blood pressure could not be obtained the last 35 minutes of the operation
15 +	G.S.W.	Ileum	1000	D	Injury to iliac and femoral vessels; the latter ligated. Sudden death 2d postoperative day. Death embolic in nature, embolus believed to come from injured vessels
16 o	G.S.W.	Small bowel	1500	I	1st postoperative day comatose. 2d postoperative day signs of pulmonary infarction developed. Good recovery
17 +	G.S.W.	Jejunum, ileum, descending colon, rectum	1500	D	Improper filtration of the blood. Gross contamination plugging needle. Embolic death on 3d postoperative day
18 +	G.S.W.	Stomach, jejunum	2000	D	Died 2d postoperative day. Autopsy revealed ruptured accessory splenic vein, hemoperitoneum, ruptured kidney and pancreas, perforation of stomach, and jejunum
19 +	G.S.W.	Stomach	2500	D	Died during operation. Associated injuries—penetration of lung, diaphragm, abdominal aorta, liver and pancreas
20 +	G.S.W.	Ileum, cecum, sigmoid	2000	D	Died during operation. Associated injuries—penetration of lung, diaphragm, abdominal aorta, liver, and pancreas
21 +	G.S.W.	Ileum	1200	I	
22 +	G.S.W.	Small bowel	1200	D	Died during operation. Associated injury—perforation of inferior vena cava
23 +	G.S.W.	Duodenum	1500	D	Died on 4th postoperative day. Autopsy revealed peritonitis, subphrenic abscess, pulmonary edema
24 +	G.S.W.	Stomach	900	I	Associated injury to liver
25 +	G.S.W.	Stomach, small bowel, colon	?	D	Died during operation. Associated injuries—ruptured spleen and liver

N.P. = Nonpenetrating.
G.S.W. = Gunshot wound.

*Reactions noted in Cases 15, 16, and 17 only; none in other cases.
I, Improved; D, died.

contaminated by hollow viscus content was used for autotransfusion.

CASE REPORTS

J. W. G., No. 2705, a 39 year old white male was admitted to the surgical service 1 hour after he had received gunshot wounds of the thigh and thorax. The entry into the thorax was on the left, at the 9th intercostal space and was followed by the vomiting of blood. On admission the temperature was 97 degrees, pulse 100, respiration 28 per minute, and the blood pressure 74/50. The patient was in shock and the abdomen was tender and rigid. A diagnosis of gunshot wound penetrating the thorax, diaphragm, and abdomen with visceral perforation and internal hemorrhage was made. Supportive treatment was given and 1½ hours following admission an exploratory celiotomy was done. There was a large amount of blood in the peritoneal cavity and perforations of the anterior and posterior aspects of the stomach were encountered. During the course of the operation the patient's condition became worse and he ceased to breathe. Coramine was given and respiration again started. Seven hundred cubic centimeters of blood which was removed from the peritoneal cavity was then administered intravenously in place of the saline infusion he had been receiving.

During the postoperative course the patient developed a wound infection and an empyema in the pleural cavity which the bullet had traversed. From both Staphylococcus albus was isolated. There was no evidence of septicemia. The patient responded well to treatment and was discharged improved on the 37th hospital day.

In this case, the reinfusion appeared to be a lifesaving procedure and there was no ill effect from the blood. It was believed that the need of blood was greater, even though it be contaminated, than the danger involved in its use.

Twenty-four more cases of abdominal trauma with hollow viscus perforation and hemorrhage have since received autotransfusion (Table IV). All but 1, which was not penetrating, were due to gunshot wounds of the abdomen. Seventeen had a fatal termination, giving a mortality of 68 per cent. Of the deaths, 6 occurred on the operating table and 6 more within the first 18 hours of the postoperative course. In all of these cases severe injuries existed and in none did death appear to have been caused by septic emboli coming from the autogenous infused blood. In 2 others, in which death occurred shortly after operation, one on the 2d day and the other on the 4th day, there was no evidence that the reinfused blood was contributory to the death. One patient died on the 84th hospital day following a very stormy course during which peritonitis and a subsequent subphrenic abscess developed. Blood cultures were persistently negative. Of the 2 remaining fatalities, death in one was directly attributed to the autotransfusion, while in the other the use of contaminated blood could not be ruled out as a contributory factor to the death.

J. S., No. 7982, a 29 year old white male, was admitted shortly after a gunshot wound of the abdomen. The patient was a well developed and nourished white male, semistuporous, in shock, and having a strong alcoholic odor to his breath. The pulse rate was 112 per minute and the blood pressure 60/30. Intravenous glucose-saline solution was started on the ward and blood crossmatched for transfusion. Two and one-half hours following admission the pressure rose to 85/50 and exploratory celiotomy was done. The peritoneal cavity contained contaminated blood and there were 8 perforations of the small bowel, 3 of the descending colon, and 2 in the rectum. During the operation approximately 2,000 cubic centimeters of blood, a large portion of which was coming from the retroperitoneal space, was removed. The blood was markedly contaminated, containing formed feces, but because of the extremely poor condition of the patient and the inability to obtain sufficient blood, 1,500 cubic centimeters was reinfused. During the infusion the needle became plugged with fecal débris, and it was found that the blood was not being properly filtered.

Sixty-two hours after operation the patient developed marked dyspnea, cyanosis, and suppression of breath sounds. One hour later signs of massive pulmonary edema developed, and death ensued shortly. At autopsy multiple pulmonary emboli and massive pulmonary edema were found.

In this case there was a definite break in technique. Gross débris was allowed to enter the blood stream giving rise to septic emboli. The bad result cannot be attributed to the procedure, but to error in the method of its use.

In the other case, death due to a large pulmonary embolus occurred on the 2d postoperative day. In this instance, there were perforations of the small bowel and severance of the femoral artery and vein. The origin of the embolus could not be definitely determined, but it was felt that it had arisen from the injured vessels.

There was but 1 reaction in the 8 cases that recovered. In this case (Case 16, Table IV) there were 4 perforations of the small bowel. At operation 1500 cubic centimeters of blood from the peritoneal cavity was returned to the patient. On the 1st postoperative day the patient became comatose, and on the 2d developed signs of pulmonary infarction. There was good recovery following the use of sulfathiazole, and he was discharged improved on the 17th hospital day.

In 4 cases, not included in this group, there was severe trauma to the kidney and in each nephrectomy was performed. In these cases the blood which was reinfused contained varying amounts of urine which had escaped from the damaged kidney. No reactions followed the use of such blood.

Hemolytic changes in the blood. Studies on blood withdrawn from the peritoneal cavity of dogs at varying intervals following intra-abdominal hemorrhage have shown that there are no changes within 6 hours following the hemorrhage. After 6 hours there is an increase in the size and shape of the erythrocytes. No hemolysis was observed before 16 hours, but after 24 hours there was a large number of destroyed red blood cells and intensive hemolysis (12). Ricci and DiPalma have found the erythrocyte count of intraperitoneal blood normal as late as 72 hours following tubal rupture. Most reactions following autotransfusion, which have been reported, have been due to the use of blood that has been in the peritoneal cavity for more than 24 hours.

In the 3 fatalities in Tiber's series (24), the blood reinfused had been in the peritoneal cavity more than 72 hours. Coley used blood which had been in the peritoneal cavity for 5 hours following rupture of the spleen. On the 2d day that patient's urine was port wine color but there were no other signs of reaction and the patient made a good recovery.

In the series here reported, in only 1 instance was blood used for autotransfusion that had been in a serous cavity for more than 24 hours. In this case a tentative diagnosis of ruptured ectopic pregnancy was made and the patient was observed for 6 days prior to operation. On opening the peritoneal cavity approximately 1500 cubic centimeters of dark unclotted blood was found. After 400 cubic centimeters had been returned, a reaction was noted. The reaction was mild, but the type was not recorded on the chart. The postoperative period was uneventful, the temperature never exceeded 100.6 degrees, and the patient was discharged improved 16 days later.

A widely accepted explanation of the hemolytic reaction, based on the work of Baker and Dodds, is that in an acid urine the free hemoglobin is precipitated in the renal tubules. A mechanical blockage ensues, and oliguria or anuria with uremia develops. DeGowin, Osterhagen and Andersch (7) in their experimental work found that when urine is alkaline the intravenous injection of a large amount of dog hemoglobin into dogs seems to be innocuous. When the urine is acid, transfusions of hemoglobin sooner or later produce renal insufficiency and it appears to be the result of the obstruction of the tubules with masses of pigment derived from hemoglobin, thus substantially confirming the experiments performed on rabbits by Baker and Dodds.

Further study by DeGowin, Warner, and Randall (8), on the human kidney following fatal transfusion reactions, revealed the same process present but to a lesser degree and that, although renal insufficiency in some cases may be due to mechanical blockage, in the majority it is probably due to a nephrotoxic substance which causes degeneration of the tubule epithelium and interstitial edema.

De Nevasquez was unable to find evidence of tubule obstruction in fatal cases following transfusion, or in animals after injection of hemoglobin, and concluded that the changes in the so called "transfusion" kidney do not appear to support the view that simple mechanical blockage of the tubules by altered blood pigments is responsible for the anuria seen in fatal cases of blood transfusion.

Although the pathologic physiology which occurs when hemolyzed blood is given intravenously is not agreed upon, it is well established that it may be toxic and under certain conditions fatal.

Hemolysis of the blood should limit the procedure but very little. Seldom is there massive internal hemorrhage that goes for

TABLE V.—MORTALITY TABLE

Type of case	No. of cases	No. of deaths	Mortality per cent
Ruptured ectopic pregnancy	22	0	0
Penetrating wounds of thorax	19	6	31.5
Nonpenetrating wounds of the abdomen	21	5	23.8
Penetrating wounds of abdomen	38	19	50.0
Without hollow viscus perforation	13	2	15.3
With hollow viscus perforation	25	17	68.0
Combined cases	100	30	30.0

more than 24 hours without operation or death ensuing. In those cases that do, there is time to obtain sufficient quantities of blood to replace that which has been lost.

SUMMARY

One hundred cases of autotransfusion following internal hemorrhage are reported in this paper. In 22, hemorrhage was due to ruptured ectopic gestation, while in the remaining 78, penetrating and nonpenetrating trauma to the thorax and abdomen was the etiological agent. There were 30 deaths in this group, making a mortality of 30 per cent. All of the deaths occurred in the traumatic cases, giving this group a mortality of 38.4 per cent. By dividing the traumatic cases into groups in respect to the type and location of the trauma, the following is found: In 19 penetrating wounds of the thorax there were 6 deaths, a mortality of 31.5 per cent. In 21 cases of nonpenetrating wounds of the abdomen there were 5 deaths, a mortality of 23.8 per cent. Nineteen deaths occurred in the 38 penetrating abdominal wounds, the mortality being 50 per cent. The highest mortality, 68.0 per cent, occurred in abdominal wounds with hollow viscus perforation. In 25 cases, 17 terminated fatally. In all but 1 of these, injury was due to gunshot wounds and hemorrhage was greater in this group than in the others (see Table V).

One fatal reaction occurred in the 100 cases, giving a percentage of 1.0. In this case there was a break in the technique of filtering the blood. In 2 other instances there were reactions from which the patient recovered, giving a combined percentage of 3.0 for reactions. There was a doubtful reaction in 1 case, but it could not be definitely established that this was due to the reinfused blood. In 1 case, the patient had no reaction from the autogenous blood but had severe reactions on 2 occasions from blood obtained from the bank (Case 1, Table IV).

It has been shown that some danger accompanies the use of autogenous blood, especially the use of contaminated blood. Sterile compatible blood from a donor source is safer, but it must be in sufficient quantities without delay and it must be remembered that 500 cubic centimeters is the donor's dose and not the recipient's. The use of autogenous blood, even though it be contaminated, is safer than allowing the blood volume to remain depleted.

CONCLUSIONS

1. Hemorrhage is the greatest single factor in the mortality of wounds of the serous cavities.

2. Autotransfusion is a valuable adjunct in the treatment of internal hemorrhage.

3. With armies in the field and trauma on the increase due to high velocity vehicles, both in military and civilian life, this procedure should be held in a foremost place in the minds of those doing emergency surgery.

4. A simple suction apparatus is described which is more efficient in the collection of blood than mopping it from the body cavities.

5. The technique, particularly as regards filtration, must be rigid.

6. Bile mixed with blood, due to injury of the liver or biliary tree, and bacterial contamination, due to hollow viscus perforation, add danger to the procedure; however, this danger is not so great as might be thought and the need of blood is frequently far greater than the danger involved.

7. Old blood, because of hemolytic changes, should not be used.

8. Alkalinization of the urine may prevent reactions caused by partial hemolysis of the blood.

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TRIPHALANGEAL THUMB

Report of Six Cases

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THE rarity of the triphalangeal thumb[1] warrants recording of 6 additional cases. Although several case reports can be found in the literature, it must still be considered as a rather infrequent anomaly. Dr. M. Pomeranz, roentgenologist of the Hospital for Joint Diseases, has informed the authors that during the past 25 years there has not been a single case of triphalangeal thumb seen in his department.

In the first 3 cases reported here the men were seen a few months apart during daily examinations of draftees. No similar cases were encountered among more than 75,000 other men who had physical examinations, despite the fact that the authors were on constant lookout for anomalies.

In the fourth case, the patient was the father of one of the draftees and was examined in the office of the senior author.

Frere (1930) reported one case exactly like Case 2 to be described by the writers. In this case, a male negro, both thumbs were affected and his mother had one similar abnormal thumb. Both thumbs of the grandmother also were said to be triphalangeal.

Haas (1939) gave histories of 3 families in which 1 or more members possessed triphalangeal thumbs.

The cases of triphalangism of the thumb reported in the literature prior to 1915 were reviewed by Stieve (1915). In addition, he presented a case of bilateral triphalangeal thumbs associated with congenital atresia ani in a 19 year old male. No other members of the patient's family had any deformity of their hands. A drawing of the roentgenograms, in dorsipalmar view, is exactly like that in Case 1 (Fig. 1).

[1]It is interesting that triphalangism of the hallux has also been seen though it is of even greater rarity than of the pollex.

From the Recruiting and Induction Station, United States Army, New York.

REPORT OF CASES

CASE 1. R. W., white male, aged 30 years, was examined by the writers at the Induction Station. He was a baker by occupation and experienced no difficulty in performing his work. No history of any similar deformity in his family could be obtained. His physical examination was entirely negative except for both thumbs; these were slightly longer than usual. The tip of each thumb reached to the level of the middle of the proximal phalanx of the index finger.

The nail phalanx of each thumb was held in slight palmar flexion and ulnar deviation pointing toward the index finger. On palpation, the impression was gained that there was an additional phalanx interposed between the basal and nail phalanges of both thumbs. The roentgenogram of the thumbs on dorsipalmar exposure (Fig. 1) showed that the head of the proximal phalanx had two well outlined condyles on its radial and ulnar sides. There was a wedge-shaped ossicle, 9 millimeters long and 7 millimeters wide (the width being measured from the apex of the wedge to its base), interposed only between the radial condyle of the head of the proximal phalanx and the corresponding radial half of the nail phalanx. The ulnar condyle of the head of the proximal phalanx, however, articulated directly with the ulnar side of the nail phalanx. Correspondingly, the base of the nail phalanx was somewhat broader than usual and had two facets forming an angle of about 150 degrees pointing proximally, one ulnar facet for the proximal phalanx and the other, the radial facet, for the middle phalanx.

The lateral view (Fig. 2) showed the same wedge-shaped ossicle interposed mainly on the dorsal aspect of the interphalangeal joint of the thumb. The proximal phalanx appeared to be of normal shape and proportions. A normal radial sesamoid was present at the first metacarpal head of both thumbs. The first metacarpals appeared to be slightly smaller and thinner than would be expected. The bones of the other fingers and wrists presented no abnormalities. Likewise, the feet (which were not roentgenographed) appeared to be normal.

CASE 2. O. S., colored male, aged 27 years, was also seen at the Induction Station. He was a carpenter by trade, and his anomaly did not interfere with his work. Except for his thumbs, the man was a well built, muscular, and apparently healthy individual. Questioning revealed a similar bilateral deformity only in his father, who was deceased. His

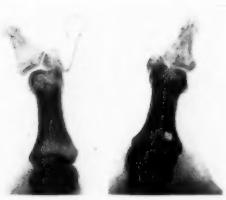

Fig. 1. Case 1. Dorsipalmar view of both thumbs: a, left; b, right. Note the wedge-shaped "middle phalanx" interposed between the radial half of the nail phalanx and the basal phalanx. The ulnar half of the basal phalanx and the ulnar half of the nail phalanx articulate directly with each other. The punctate outline reconstructs what may be the absent distal part of the nail phalanx of an apparently bifid thumb.

nine sisters and two brothers were said to have normal hands.

On examination, both thumbs were found to be unusually long; when the thumbs were held close to the index, their tips extended almost to the level of the proximal interphalangeal joint of the index finger. Three definite phalanges with proximal and distal interphalangeal joints were present in each thumb. The nail phalanx of each thumb was held in palmar flexion at about 135 degrees so that its tip pointed toward the index finger. The proximal phalanx of the thumbs was unusually long, measuring about 4 centimeters on the roentgenogram (Fig. 3). The middle phalanx was small, measuring 15 millimeters on the right and 12 millimeters on the left side, both being trapezoid shaped, especially the left. Each nail phalanx appeared to bermal, and no was 2 centimeters long in both thumbs.

Grossly, there was normal mobility of both thumbs, which could be opposed and flexed in normal fashion. Motion in the metacarpophalangeal joints was possible between 180 degrees of extension and 90 degrees of palmar flexion. The proximal interphalangeal joint could be moved between 170 degrees and 100 degrees of palmar flexion. The distal interphalangeal joint had the least range of motion, being between 135 and 125 degrees of palmar flexion. The lesser fingers and both hands presented no other abnormalities, except that the thenar eminences were slightly flatter than in a normal hand. Both wrists and all other joints of the body, including the feet, were normal.

CASE 3. J. G., white male, aged 19 years, was examined at the Induction Station. He was a clerk by occupation. Triphalangism of both thumbs was noted in combination with bilateral congenital absence of the pectoralis major and minor muscles and slight pectus excavatus. The young man stated that his father had similar thumbs.

Examination revealed that the boy was fairly well nourished and fairly well built except for a round shoulder deformity. There was a congenital bilateral absence of the pectoralis major and minor muscles, more pronounced on the left side. His feet were well

Fig. 2. Case 1. Lateral view of both thumbs: a, left; b, right. Note the wedge-shaped "middle phalanx" interposed between the basal and nail phalanges on the dorsal and radial aspects. Note also that the basal phalanges appear to be normal, while the first metacarpal may be slightly smaller and thinner than normal.

formed and presented no abnormalities. The second toes were slightly longer than the big toes, as in average normal feet. No roentgenogram of the feet was taken.

Examination of the hands revealed they were of the long and rather narrow type, and in a relaxed attitude, both hands were held in slight radial deviation at the wrist joints (Fig. 8).

Roentgenogram (Fig. 4) of the wrists showed that the lower end of the ulna extended slightly more distally than that of the radius, unlike the reverse

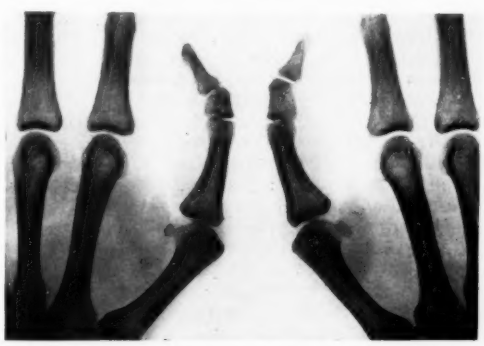

Fig. 3. Case 2. Dorsipalmar view of both hands with the thumbs—a, left; b, right—shown in oblique view. Note the excessive length of both thumbs which reach almost to the level of the proximal interphalangeal joint of the index. Note also the ulnar deviation of the nail phalanx of both thumbs with trapezoid-shaped middle phalanges, especially on the left side. The middle phalanx of the right thumb is larger, with its articular surfaces more parallel to each other, and it appears more like a normal phalanx.

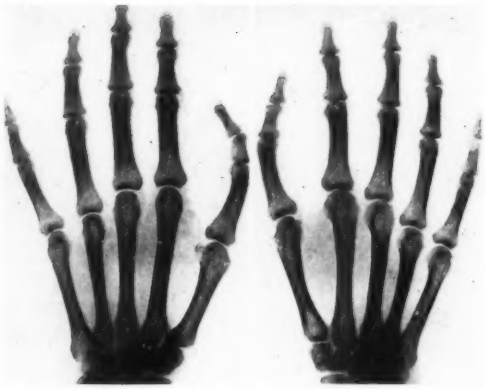

Fig. 4. Case 3. Dorsipalmar view of both hands: a, left; b, right. Note the trapezoid-shaped appearance of the middle phalanges (especially on the left) with radial deviation of the distal part of the triphalangeal thumbs. Note also that the second metacarpal head extends more distally than the third. Likewise, the ulnar styloid is more distal than the radial styloid.

relationship in a normal adult human wrist. This was somewhat more marked on the right side and apparently was responsible for the radial deviation of the hands. The carpal bones appeared to be essentially normal.

The thumbs were unusually long, especially the right. The tip of the right thumb reached to the level of the distal interphalangeal joint of the index finger, while that of the left thumb reached to the proximal interphalangeal joint of the index. The distal two phalanges of both thumbs were held in slight palmar flexion and also were deviated ulnarward, pointing to the index finger. This was more pronounced on the left side. Both thenar eminences were much flatter and longer than normal.

True opposition of both thumbs was absent so that the palmar surface of the tip of the thumb could not be placed parallel to the palmar surface of the lesser fingers, both of these planes forming an angle of 90 degrees in full opposition. The prevailing active motion of both thumbs was that of palmar flexion, produced by the flexor pollicis longus.

The web between the first and second fingers was located much more distally than in a normal hand, being almost at the level of the metacarpophalangeal joint of the index on the right side, and slightly proximal to it on the left side.

The range of motion of both wrists and fingers was similar on both sides. The metacarpophalangeal joint of the thumbs could be hyperdorsiflexed to 35 degrees beyond neutral and palmarly flexed to an angle of 90 degrees. The proximal interphalangeal joints of both thumbs were in fixed palmar flexion of 165 degrees and could be further palmarly flexed to 50 degrees. The distal interphalangeal joint was the least movable, motion being

Fig. 5. Case 3. Dorsipalmar view of both thumbs—a, left; b, right—illustrating especially the trapezoid shape of the middle phalanx with ulnar deviation of the distal part of the thumb, more marked on the left side.

possible between 180 and 140 degrees. There was definite limitation of palmar flexion at the second, third, and fourth metacarpophalangeal joints, especially at the second. Hyperdorsiflexion at the metacarpophalangeal joints of the index, third, fourth, and fifth fingers was possible to 30 degrees, 20 degrees, 10 degrees, and 15 degrees beyond neutral, respectively. Palmar flexion in these joints listed in the same order was possible to an angle of 150 degrees, 110 degrees, 120 degrees, and 85 degrees, respectively. The range of motion at the proximal and the distal interphalangeal joints of the lesser fingers was normal, except for a few degrees of limitation of dorsiflexion at the proximal interphalangeal joints of all the lesser fingers.

The right radial pulse was not felt in its usual location, but could be palpated along the middle line on the palmar aspect of the forearm just above the wrist. On the left side the pulse was present in its normal location.

The roentgenogram of both hands on dorsipalmar view (Fig. 4) showed that the right first metacarpal was considerably longer than the left, being mainly responsible for the comparatively increased length of the right thumb. It is interesting to note that the second metacarpal heads extended farther distally than the third, not as is found in an average human hand. In spite of this the third digit was the longest on both hands, 0.5 centimeter longer than the index.

Both thumbs had three well formed phalanges. The nail and the proximal phalanges presented no definite abnormalities. Likewise, the middle phalanx of the right thumb was somewhat similar in its size and shape to that of the fifth finger. The middle phalanx of the left thumb, however, was definitely trapezoid shaped and was somewhat shorter and stouter than that on the right. Slight palmar flexion and radial deviation of the distal part of the thumbs were evident. The trapezoid shape of the middle phalanx of the left thumb and ulnar deviation of the distal part of both thumbs were especially clearly demonstrated on dorsipalmar view of the thumbs themselves (Fig. 5).

Case 4. I. G., white male, aged 51 years, father of J. G., was a paper cutter by trade and was not

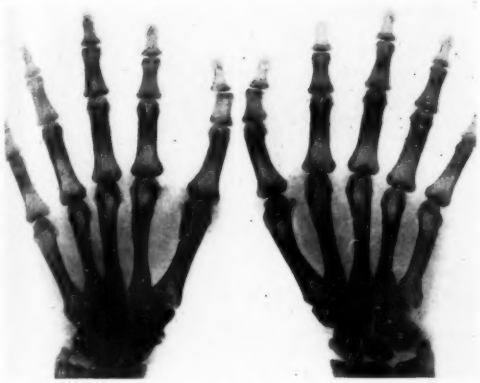

Fig. 6. Case 4. Dorsipalmar view of both hands, with similar findings as described in Figure 4. Note that the second metacarpal head extends somewhat more distally than the third, especially on the left side. The relatively greater length of the styloid of the ulna is more marked than in Case 3. In addition, there are bilateral bipartite navicular bones (not a fracture). Slight productive osteoarthritic changes are present between the left navicular and multangulum majus on the left side.

handicapped by the anomaly of triphalangism of his thumbs. He stated definitely that none of his four brothers and three sisters, nor his father and mother and both grandparents had any abnormalities of their hands and feet. J. G., his son, was the only other member of his family having triphalangeal thumbs. The one brother of J. G. had normal hands and feet.

At the age of 12, I. G. gradually developed considerable scoliosis. Prior to this age his back was said to be perfectly straight.

Examination revealed a small, elderly man with very marked right dorsal scoliosis. There was considerable asymmetry of the chest, the left ribs being more prominent anteriorly than the right. This was apparently related to the scoliosis and was not congenital. There was complete bilateral absence of the pectoralis major and minor muscles. The feet were essentially negative, except for bilateral absence of pulsation of the posterior tibial arteries, which was apparently an anatomical variation and not an arterial occlusion.

Both hands of I. G. presented essentially the same appearance as those of his son (Fig. 9). Both thumbs were triphalangeal, and the thenar eminences were poorly developed. The tips of the thumbs reached to the level of the distal interphalangeal joint of the index fingers. Both thumbs were of about the same length, except that the left appeared to be a few millimeters longer.

The web between the first and second fingers was at the level of the metacarpophalangeal joint of the thumbs.

The range of motion of the right and left thumbs was similar. Dorsiflexion at the first metacarpophalangeal joint was possible to 10 degrees beyond neutral and palmar flexion to 90 degrees. The proximal interphalangeal joints could be dorsiflexed to 5 degrees beyond neutral and palmarly flexed to an angle of 80 degrees. At the distal interphalangeal joint motion was possible from 180 to 160 degrees of palmar flexion.

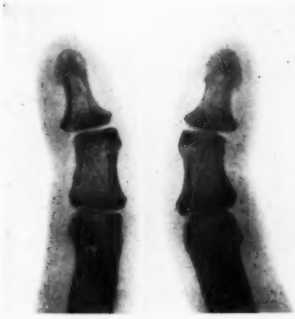

Fig. 7. Case 4. Dorsipalmar view of both thumbs, showing moderately trapezoid-shaped middle phalanx with radial deviation of the distal part of the thumb.

Active opposition of the thumbs was lost the same as in the son's hands. The father's hands, like the son's, also presented some restriction of palmar flexion at the metacarpophalangeal joints of the lesser fingers. The metacarpophalangeal joints of the second, third, fourth, and fifth fingers each could be dorsiflexed to 10 degrees beyond neutral and palmarly flexed to 100 degrees, 90 degrees, 90 degrees, and 85 degrees, respectively. The motion of the interphalangeal joints of the lesser fingers was normal.

No arterial pulse could be palpated anywhere on the palmar or dorsal aspect of either wrist or lower third of forearms.

A roentgenogram of both hands on dorsipalmar view (Fig. 6) showed that both thumbs had three phalanges. The proximal and the nail phalanges of both thumbs resembled those of the lesser fingers. The middle phalanx, however, was much stouter and somewhat shorter than the middle phalanges of the lesser fingers. It also differed from them because of its slight trapezoid shape. These special features of the middle phalanx of the thumbs were especially evident on dorsipalmar view of the thumbs (Fig. 7), which also showed slight ulnar deviation of the nail phalanx (although not as marked as on the left thumb of the son).

Both first metacarpals were about the same length. The second and third metacarpal heads of the right hand appeared to extend distally to about the same level. The left second metacarpal head extended about 2 millimeters more distally than the right. However, both third fingers were the longest. Roentgenogram of the wrists (Fig. 6) showed marked development of the styloid of the ulna, which was longer than that of the radius, the styloid process of

Fig. 8.

Fig. 9.

Fig. 10.

Fig. 8. Case 3. Photograph of hands.
Fig. 9. Case 4. Photograph of hands.
Fig. 10. Case 5, R. G. Photograph of both hands showing bifid left thumb. The left ulnar thumb has a normal appearance and has two phalanges. The left radial thumb is smaller and is triphalangeal.

the latter appearing somewhat underdeveloped. All of these were even more pronounced in the father than in the son. In addition, both navicular bones were bipartite in the father.

CASE 5. R. G., a white printer, aged 24 years, was seen at the Induction Station. He had a congenital deformity of the left thumb only. There was no history of any deformities of hands or feet in the known members of his family for three generations. In addition to the left thumb deformity he had a draining pilonidal sinus. One of his brothers also had a pilonidal sinus. The draftee was a well built, somewhat overweight, apparently healthy young man. His penis was underdeveloped. Likewise, both of his testicles were very small, the size of a small grape, although both of them were fully descended into the scrotum. He reported practically complete lack of sexual desire. Mentally he was normal. Both of his feet appeared to be perfectly normal except for mild pes planus (no roentgenograms of feet were taken).

The left thumb was bifid with two well developed nails (Fig. 10). There was a skin web connecting the two thumbs almost down to the distal phalanx. The roentgenogram of both hands (Fig. 11) showed an apparently normal left first metacarpal which articulated with the two basal phalanges spreading in V-shape manner. The basal phalanx of the ulnar thumb was of approximately normal size and shape and articulated with a normal nail phalanx. The basal phalanx of the radial thumb was much shorter and slenderer than that of the ulnar thumb. It continued into the middle and nail phalanges in the radial thumb, both of which were rather small and thin. The middle phalanx of the radial thumb formed almost a right angle with its basal phalanx. Well developed proximal and distal interphalangeal joints of the radial thumb were demonstrable. Otherwise the roentgenogram of the hands presented no abnormalities. The third metacarpal head on both sides extended slightly more distally than the corresponding second metacarpal head. The styloid of the ulna on both right and left sides extended slightly more distally than did the styloid of the radius.

Motion at the "compound" left first metacarpophalangeal joint was limited, being possible between 180 and 150 degrees of palmar flexion. The entire bifid thumb moving *in toto*. The same limited range of motion was also present in the right first metacarpophalangeal joint. Motion at the interphalangeal joints of both left thumbs, the two phalangeal, and the triphalangeal, was almost completely absent, being reduced to a slight wobble. Opposition of the left thumb, mainly of its ulnar component, was normal.

CASE 6. A white male, aged 25 years, was examined at the Induction Station. There was no history of any deformities in his family. He was a well built, healthy young man and presented no abnormalities other than his left thumb. The latter was very short and formed almost a right angle with the long axis of the hand. Motion of the right thumb was somewhat restricted.

The roentgenogram of both hands (Fig. 12) shows that the left first metacarpal was only slightly shorter than the right. The nail phalanx of the left thumb was approximately of the same size and configuration as that of the right thumb. A short square ossicle, evidently the proximal phalanx of the thumb, articulated with the nail phalanx distally and with the radial part of the first metacarpal head, proximally. There was another triangle-shaped ossicle articulating with the ulnar part of the first metacarpal head. This ossicle was located just ulnarward to the diminutive proximal phalanx hugging the latter at its ulnar surface. Two sesamoids were present over the palmar aspect of the first metacarpal head of each thumb, and a radial sesamoid was present over each second metacarpal head. At first glance one had the impression that the left thumb had three phalanges. However, comparison of the left thumb of Case 6 with a typical bifid thumb (Fig. 13) suggests an entirely different interpretation.

Apparently the left thumb in Case 6 may also be looked upon as a bifid thumb in which the two phalanges of the radial thumb and only a part of the basal phalanx (the trian-

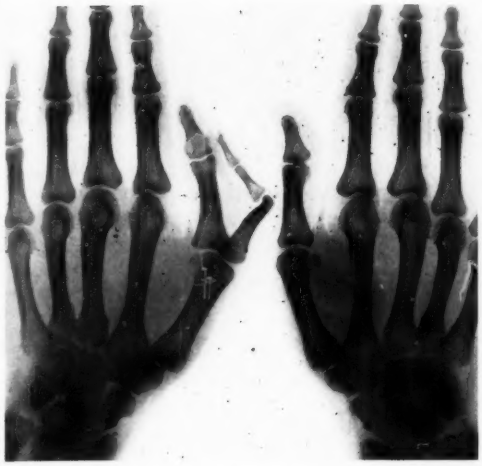

Fig. 11. Case 5, R. G. Roentgenogram of both hands showing triphalangeal left radial thumb, a, left. Note that the styloid of the ulna extends slightly more distally than that of the radius.

gular ossicle) of the ulnar thumb have been retained, while the nail phalanx of the ulnar thumb has been lost. Case 6 bears a great similarity to Case 1, both apparently presenting atypical bifid thumbs, and not a triphalangism of the thumb. In Case 1, however, only the nail phalanx was bifid, while in Case 6 the division was more extensive so that both the nail and the proximal phalanx were bifid.[1]

ETIOLOGY AND ORIGIN OF TRIPHALANGISM

It is not within the scope of this paper to go into a detailed discussion and review of the extensive literature on the etiology and origin of triphalangism of the thumb. Numerous speculative hypotheses have been advanced, none of which seems to be sufficiently substantiated.

The theory of phylogenetic origin of triphalangism of the thumb seems to be the weakest.

According to Morton (1935), "the number of phalanges in ancient amphibian digits was quite variable but yielded a subsequent reptilian formula of 2, 3, 4, 5, 4. . . . The phalangeal bones of the digits tended toward a reduction in the feet of some of the ancient reptiles; and, of particular significance, within the mammal-like therapsid group the phalanges were reduced to the characteristic mammalian formula of 2, 3, 3, 5, 3."

Even in the lowest scale of modern animal life, as amphibians, the two phalangeal formula of the first digit is firmly established. Therefore, it seems to be too much of a stretch of the imagination to consider the triphalangeal thumb as a reversion to the more primitive condition.

Some regard the two phalangeal formula of the thumb as a result of disappearance of one of its phalanges. Others look upon the first metacarpal as a basal phalanx and assume that the thumb has lost its metacarpal bone. Galen (130–200 A.D.), quoted by Mueller (1937), was one of the earliest proponents of the latter view.

The peculiarity of the epiphysis of the first metacarpal, which, as a rule, develops only at its base, similarly to the epiphyses of the phalanges, seems to afford some support to the consideration of the first metacarpal as a phalanx. However, this concept is undermined by the existence of numerous cases with a capital epiphysis present in addition to the basal epiphysis at the first metacarpal.

Regardless of whether the first metacarpal is considered a true metacarpal or a basal phalanx, both of these views are untenable as

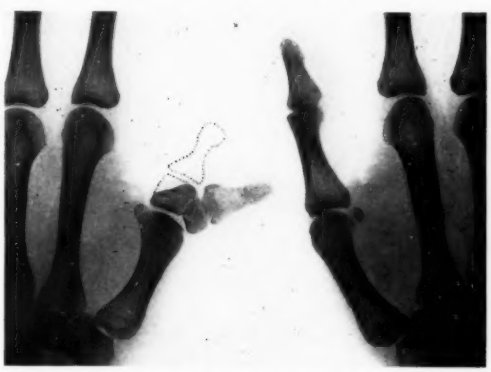

Fig. 12. Case 6. Evidently a bifid right thumb, simulating triphalangism. The punctate outline reconstructs the part of the basal phalanx and the nail phalanx of the right ulnar thumb which probably have failed to develop.

[1] Later the authors expect to publish their observations in a number of cases of bifid thumbs of varied extent of division. It is their opinion that this anomaly is not a rarity.

Fig. 13. Dorsipalmar roentgenogram of a right bifid thumb with division extending through the nail and proximal phalanges.

explanations for triphalangism of the thumb, since the two phalangeal formula (two phalanges and a metacarpal, or three phalanges without a metacarpal) is constant in the first digit of all forms of animal life from the amphibians up.

It is difficult to conceive of the presence of the third phalanx as resulting from lack of fusion of the epiphysis of one of the phalanges of the thumb, since there are true joints separating the middle phalanx from the other two phalanges in a triphalangeal thumb. There is no known instance of formation within epiphyseal cartilage of a true joint with articular facets lined with hyaline cartilage and a joint capsule.

In addition, the lack of evidence for triphalangism of the thumb both in early embryonal development and in fossil specimens of higher vertebrates also speaks against these two theories.

Joachimsthal (1900) advanced the belief that some instances of triphalangeal thumb represented a duplication of the index finger with absence of the thumb. Similarly, Graefenberg (1914) postulated that the hand with a triphalangeal digit on the radial side of the four lesser fingers should be interpreted as one with the thumb absent and with a part of another hand added instead of the lost thumb.

These interpretations may perhaps be applicable only in those comparatively few recorded cases (see Figs. 4 and 5, Case 2, Cohn, 1932), in which there was no evidence of the usual characteristics of the thumb, such as the well developed specialized musculature of the thenar eminence. However, it appears that cases of true thumbs with three phalanges, as are the majority of cases recorded in the literature, including the 6 reported here, can hardly be explained by these theories.

To account for the presence of fully developed thumbs with three phalanges, the possibility of some congenital or hereditary disorientation of the germ plasm, as advanced by some writers, seems a more plausible postulation, although evidence is lacking to make it conclusive.

Haas (1939), in a study of three families, made the interesting observation of longitudinal splitting of the distal part of the nail phalanx, giving it a peculiar "duck-bill" appearance. A similar "duck-bill" appearance of the right thumb is present in Case 3 (Fig. 6) of Cohn's (1932) series. In none of the cases reported here was the "duck-bill" division of the nail phalanx present.

Haas states: "The explanation offered for this anomaly of a three-phalangeal thumb is that it may be an arrested attempt to form an extra thumb." It seems to the authors that the "duck-bill" appearance should be interpreted rather as a tendency toward the formation of a bifid thumb (Figs. 10, 11, 13).

Cases of bifid digits or longitudinal division of the digital rays, including the thumb, leading to their duplication are well known (Fig. 13). The extent of this division varies from slight longitudinal splitting of the distal part of the nail phalanx ("duck-bill" appearance described by Haas) to actual presence of two separate nail phalanges, or even complete duplication of the entire digit, including the metacarpal. The two members are then in the same relation to each other as the object to its mirror image (Fig. 13).

Figures 1 and 12, showing a dorsipalmar view of the left thumb of Case 1 and that of Case 6 are suggestive. In Case 1 (Fig. 1) the punctate outline reconstructs the absent distal part of the nail phalanx of a bifid thumb, only the

base of which is present and simulates a middle phalanx of the thumb. In Case 6 (Fig. 12) the punctate outline represents the missing parts of the proximal and nail phalanges. Note that in Cases 2, 3, and 4 (Figs. 3, 5, and 7), and also in cases reported by numerous other observers, both middle phalanges appear wedge-shaped or more or less trapezoid-shaped. It is possible to assume that in Cases 2, 3, and 4 the middle phalanx also represents a part of the base of an additional nail phalanx. This base, however, became completely interposed between the nail and the basal phalanges of the thumb, and therefore lost its wedge-shaped appearance as in Cases 1 and 6, assuming a trapezoid shape instead. The middle phalanx of the right thumb in Cases 2, 3, and 4 (Figs. 3, 5, and 7) seems to illustrate a further step in the same process. The middle phalanx became elongated, with its two articular surfaces becoming more parallel to each other and appearing more like a normal phalanx. The dorsipalmar view of the thumbs in Case 1, the left thumb in Case 3, and the right thumb in the same case may be considered as representing different stages in this metamorphosis of the "middle phalanx" from a wedge-shaped ossicle (Fig. 1) through the markedly trapezoid shape (Fig. 5, left thumb), and finally to an almost normal appearing phalanx (Fig. 5, right thumb).

The almost constantly present ulnar deviation of the distal part of the triphalangeal thumb may also be interpreted as favoring the above theory. It can be assumed that the distal part of the radial member in a bifid thumb was lost, while the ulnar member remained, retaining its original ulnarward pointing position. In Case 6 (Fig. 12) apparently the radial member of a bifid thumb was retained while only a part of the basal phalanx of the ulnar thumb remained.

The hereditary tendency in the occurrence of congenital anomalies of the limbs, including triphalangism of the thumb, is a well established fact, noted in a majority of the recorded cases, and illustrated by 3 of our cases (Cases 2, 3, 4).

The frequency of the occurrence of a combination of triphalangeal thumb with a bifid thumb (Figs. 10, 11) and also with various other congenital malformations in the same individual or in different members of the same family has also been confirmed by numerous observers. In Cases 3 and 4 the triphalangism of the thumbs was associated with bilateral congenital absence of the pectoral muscles.

The congenital division of both carpal navicular bones in Case 4 seems to be a simian feature, since the navicular bone (os naviculare and os centrale) is normally bipartite in a number of lower primates (Lapidus, 1940, Fig. 3). Likewise, the greater length of the ulnar styloid as compared with the radius also seems to be a simian characteristic.

Mueller (1936) collected 5 cases of triphalangeal thumb. In all of these cases there was also evidence of bifid thumb (one of the cases even presented the extremely rare anomaly of bilateral trifid division of the nail phalanx, in addition to triphalangism of the thumbs).

In 2 of Mueller's cases definite heredity of the anomaly could be established for four and five generations, respectively. In 1 case inquiry revealed that none of the relatives had any malformations. In the 2 remaining cases no family history was obtainable.

Most interesting is Case 4 in Mueller's series, where the paternal great grandmother and grandmother had simple triphalangism of the thumb and the patient and his father had a combination of triphalangism of the thumb with bifid thumb. In Case 5 triphalangism of the thumb on both hands was associated with doubling of the thumbs and congenital webbing of all the lesser fingers of both hands. A complete family tree for five generations showed the occurrence of triphalangeal thumbs in various combinations with radial polydactylism (double thumbs), syndactylism of the fingers and toes, congenital shortening of the index finger and congenital shortening of the fifth fingers with klinodactylism (congenital lateral deviation of the distal part of the finger) in different members of the family.

The frequent association of triphalangism of the thumb with bifid thumb (longitudinal splitting into two symmetrical parts) seems to furnish additional evidence stressing their close relationship. Consequently, it is possible that triphalangism of the thumb may be only an incomplete development of the distal part

of one of the two nail phalanges of a bifid thumb (Figs. 1, 12, 13).

If this theory is correct, then the middle phalanx of the triphalangeal thumb cannot be considered as a true middle phalanx homologous to the middle phalanx of the lesser fingers. It must be looked upon rather as a remnant of the base of an accessory nail or proximal phalanx which failed to achieve full development.

SUMMARY

1. Six cases of triphalangeal thumb have been reported. In 3 of these heredity of the anomaly could be established.

2. This anomaly must be considered rare since the first 3 cases were noted among more than 75,000 draftees examined.

3. None of the various theories advanced at present can be accepted as an adequate explanation for the cause of this anomaly.

4. From a review of the recorded cases including the 6 cases reported here it appears that triphalangism of the thumb may have at least two origins: (a) Double index or an extra finger fused on the radial side of the hand which lost its thumb, simulating the triphalangeal thumb. (b) Remnant of one of the phalanges of an incompletely developed bifid thumb, simulating a third phalanx.

5. If these two theories are correct, it follows therefore that in the first the triphalangeal digit is not a true thumb. According to the second theory, the additional phalanx is not a true middle phalanx similar to that of the lesser fingers, but a remnant of the base of one of the phalanges of a bifid thumb. The latter theory is favored by the authors.

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INSERTION OF SMITH-PETERSEN NAIL WITHOUT AN INITIAL SKIN INCISION

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THE internal fixation of intracapsular hip fractures is now of proven value. The Smith-Petersen type of nail is probably the most widely used, and numerous articles and statistics attest to the excellent results obtained.

The technique of inserting this type of nail has undergone numerous revisions as experience has been accumulated. The trend has been toward making the operation more and more simple. The method herein described for the insertion of the Smith-Petersen nail eliminates an initial skin incision and is, we believe, the simplest and easiest technique yet devised.

A number of guides have been developed to simplify the internal fixation of fractures of the hip. Several are based on the fact that the anterior wall of the femoral shaft and neck are nearly parallel with the center of the femoral neck. Examples of these are the Bailey guide, the Littig guide, the Scuderi-Callahan flange director, and the Geckeler and Tuttle[1] guide. This latter guide is for the insertion of screws, and the guide described here most nearly resembles this, being an adaptation for the use of the Smith-Petersen nail.

This procedure may be done with or without fluoroscopic control. If fluoroscopic control is the method of choice, one must be sure that there is sufficient power available in the machine and an acceptable table to give good visualization. Lateral check-up roentgenograms after reduction are also essential because of the inadequacy of the fluoroscope for this view.

The patient is placed on a casette tunnel to facilitate the sliding of the casette into place for the anteroposterior roentgenogram. This tunnel also raises the patient so that the lateral roentgenogram is more easily taken. The lateral view is taken by holding the x-ray plate at an angle away from the crest of the ilium, as has been frequently described.

We prefer spinal anesthesia of about 40 to 50 milligrams of novocain crystals or its equivalent for this particular procedure. In old people this is an adequate dose, if given correctly. This small dose seldom causes any marked drop in blood pressure. The period of anesthesia is short, but long enough for this operation. The relaxation obtained is ideal.

We reduce the fractured hip by the Ledbetter maneuver and take an anteroposterior and a lateral roentgenogram to make certain the reduction is good. Complete anatomical reduction of intracapsular fractures of the hip is most often easily accomplished and is practically always possible; therefore, the nailing of an inadequately reduced hip is a serious mistake indeed. After reduction, the leg is held by an assistant throughout the procedure in marked internal rotation and moderate abduction. Usually the marked internal rotation of the extremity brings the neck of the femur into a plane parallel, or closely parallel, to the top of the operating table, which helps to make the procedure technically easy.

While the check-up x-ray plates are being developed, the site of operation is prepared with an antiseptic. A cloth wet with bichloride solution is then placed over the field and is left in place during the entire procedure. This gives added protection against infection. The usual draping is done after this cloth is in place.

If the check-up roentgenograms show good reduction, we are ready to proceed with the operation. We use a simple instrument, consisting of a Steinmann pin, a block of steel with parallel holes drilled through it, and a small caliber trochar. The block of steel has three parallel holes bored through it, one the diameter of the trochar, and two the diameter of our Steinmann pin. The center of the latter two holes are $\frac{5}{8}$ of an inch and $\frac{13}{16}$ of an inch from the center of the hole having the diameter of the trochar. In cases of extra large bones, we use the holes farthest apart; in all other cases the holes closer together are used.

We place a towel clip deeply into the anterolateral aspect of the thigh and with strong traction pull the belly of the vastus lateralis muscle forward. This makes the shaft of the femur just distal to the trochanter, which is the optimum

From the Department of Surgery of Western Reserve University School of Medicine, and the Fracture Service of Cleveland City Hospital. Presented as a moving picture at the meeting of the Central Surgical Association, Chicago, February, 1942.

[1]Geckeler, E. O., and Tuttle, A. Surg. Gyn. Obst., 1941, 72: 106–111.

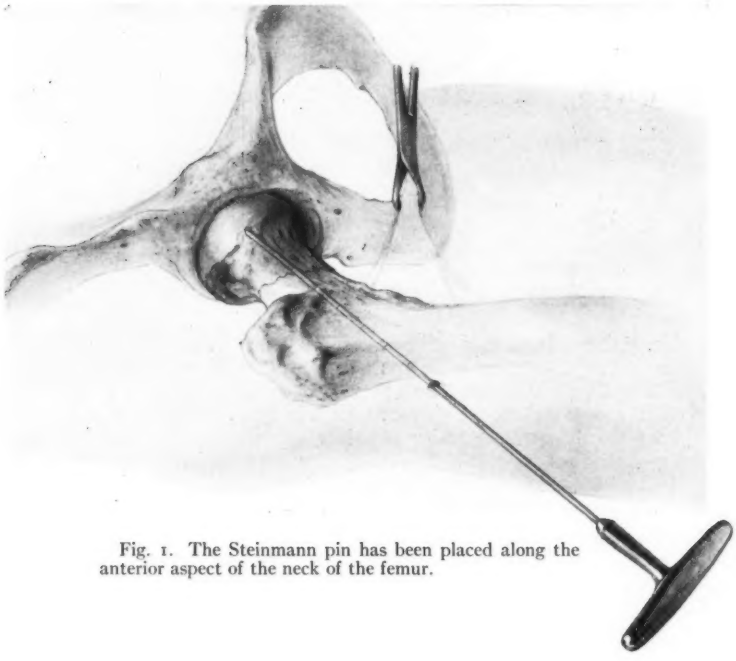

Fig. 1. The Steinmann pin has been placed along the anterior aspect of the neck of the femur.

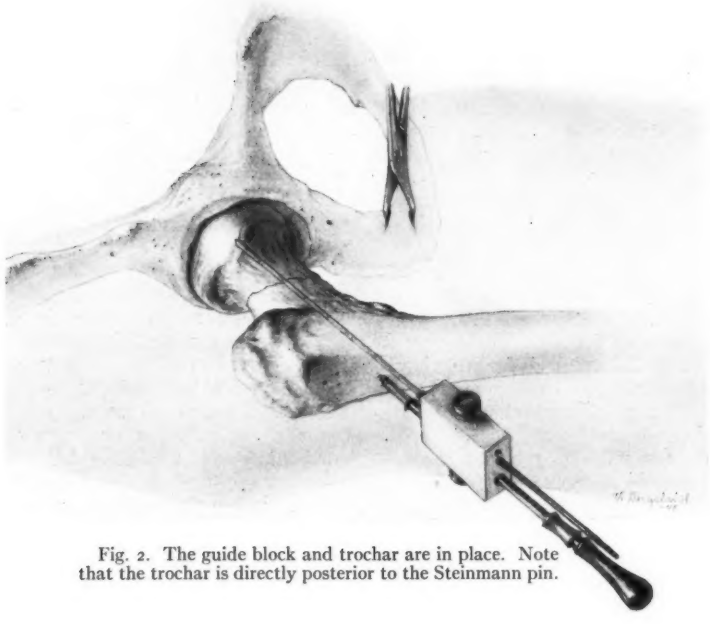

Fig. 2. The guide block and trochar are in place. Note that the trochar is directly posterior to the Steinmann pin.

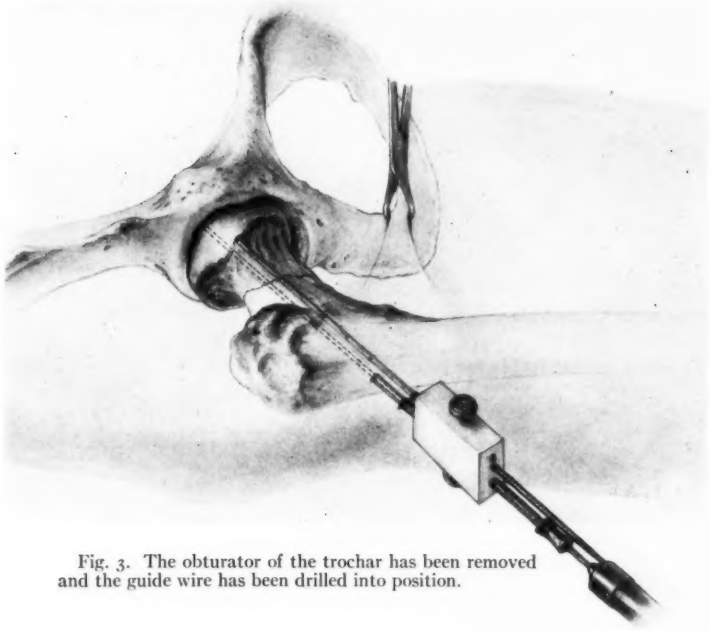

Fig. 3. The obturator of the trochar has been removed and the guide wire has been drilled into position.

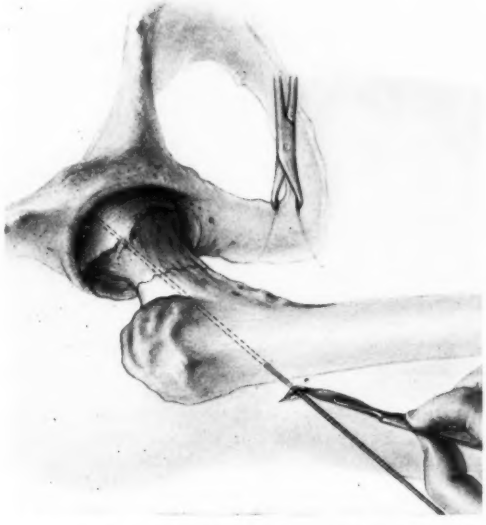

Fig. 4. The instrument has been removed and the guide wire for the Smith-Petersen nail is in place.

Fig. 5. The Smith-Petersen nail is shown in proper position.

Fig. 6. Immediate results in the first 16 cases. Approximately 60 cases have now been done with equally good results.

location for the nail, more easily palpable, and also presents an almost avascular area through which to operate.

The Steinmann pin, used as a probe, is thrust through the skin and along the middle of the anterior portion of the neck of the femur (Fig. 1). A chuck handle is used to make the handling of the pin more easy. If the pin digresses to either side of the neck, this can be felt as can also the solid bone if the pin is properly inserted. The point of the Steinmann pin is pushed hard against the head of the femur when its resistance is met. Fluoroscopic visualization of this entire procedure makes it extremely simple. If the operation is being done blindly, an anteroposterior roentgenogram is taken at this point to be sure that this important guide (the Steinmann pin) has been properly placed. This Steinmann pin is grooved each half inch so that the length of Smith-Petersen nail which will later be required

Fig. 6—Continued

can be computed easily on examination of the roentgenogram.

The steel guide block is now threaded on the Steinmann pin up to the skin and is so placed that the hole for the trochar lies directly posterior. The trochar is placed through this hole and thrust through the skin and hard against the shaft of the femur (Fig. 2). The obturator of the trochar is hit sharply so as to dent the hard femoral shaft; after this has been done the obturator of the trochar is removed.

A guide wire for the Smith-Petersen nail, which is 10½ inches in length and $\frac{3}{32}$ of an inch in diameter, is now threaded through the trochar and is drilled into place if the fluoroscope is being used. When fluoroscopic control is not being used, we usually drill the wire in about 2 inches and then pound it into its proper position (Fig. 3). The density of the femoral head can thus be detected, regulating the distance the guide wire is inserted. The guide instrument is now removed leaving the guide wire for the Smith-Petersen nail

in proper position in the neck of the femur (Fig. 4). If the foregoing operative technique has been properly carried out, this wire is bound to be in good position.

If the fluoroscope has been used, the Smith-Petersen nail to be used is determined by placing another 10½ inch wire alongside the inserted guide wire with the tip against the shaft of the femur. The difference in the apparent length of the two wires is the proper length of nail to be used.

A small skin incision is made along the guide wire, just large enough to admit the Smith-Petersen nail, which is threaded over the guide wire and driven home (Fig. 5). There is no bleeding. The guide wire is removed and the skin incision is closed with a single skin clip to complete the procedure.

The actual operating time is only a matter of minutes. With this method the position of the guide wire for the Smith-Petersen nail in the anteroposterior plane is practically certain and its position in the longitudinal plane, if the fluoroscope is used, is absolutely under the operator's visual control.

SUMMARY

The small amount of anesthesia required, the shortness of the procedure, and the absence of loss of blood all decrease the possibility of shock in these patients who are usually old. The danger of infection when this technique is used is minimal. These factors plus the extreme ease with which this simple procedure is carried out recommend it for use in either the completely equipped institution, where fluoroscopic control can easily be used, or in those institutions where only a small portable x-ray machine is available.

The procedure described has been carried out in more than 60 cases with entirely satisfactory results (Fig. 6).

THE "MALIGNANT" HEMANGIOMA

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BY the term "birthmark" is usually meant some form of hemangioma, frequently of minor importance from the standpoint of the health or appearance of the patient. Dorland, in *The American Illustrated Medical Dictionary*, defines "malignant" as "virulent, and tending to go from bad to worse." This is certainly true of many hemangiomas, a possibility that is all too frequently overlooked. Hemangiomas may be found in all degrees of severity, from small, reddish blotches and portwine stains to venous engorgements and areas filled with bright red arterial blood, which tend to grow and invade local tissues.

In infants, the arterial hemangioma must be given close consideration because of its tendency to spread, to deform or destroy features (Fig. 1), to invade deep tissues (Fig. 2), and in some instances actually to produce death. This type may certainly be termed malignant according to the above definition. All "strawberry" marks tend to grow. This growth may be so slow that many years are required for it to assume embarrassing proportions. Certainly, the average such area does not enlarge rapidly. A few may spread so rapidly that an increase in size may be apparent from week to week. The part of the body involved usually determines the seriousness of the lesion, a small area on an eyelid obviously being much more serious than a larger area over the trunk or extremities (Fig. 3).

It is stated in medical literature that such birthmarks may disappear spontaneously. Except for the light reddish, splotchy areas over the back of the neck and between the brows, frequently seen in infants, it is doubtful if such recession occurs, and never should one hopefully await this in dealing with the arterial hemangioma.

AGE OF TREATMENT

Often the arterial hemangioma appears in the first month of life, usually first as a small area, either pin-point in size or up to the size of a dime. The increase in size may be in surface area only, remaining entirely cutaneous or may be in all directions, penetrating deeper along paths of least resistance. Obviously, the proper time for treatment is as soon after appearance of the lesion as possible, especially if a feature or otherwise anatomically important area is involved.

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CHOICE OF TREATMENT

Portwine stain. This lesion involves the full thickness of the skin, is a reddish purple blotch, and grows only as the child grows. It is not sensitive to radiation, as a rule, and if radiation is tried, it must be done cautiously and abandoned as soon as it is found ineffective and before damage to the skin occurs. A goodly proportion of those patients with portwine stains have applied for treatment because of a severe radiation dermatitis present, the portwine stain not being controlled. Adequate treatment consists of the replacement of the involved skin throughout its full thickness. Oftentimes, especially in the female, it is better to advise the use of cosmetics.

The venous angioma. This consists of large channels filled with venous blood; its growth is slow. Treatment is surgical, by excision, or multiple injections with sclerosing solutions. Occasionally, the interstitial use of radon is helpful.

The arterial angioma. This paper is primarily concerned with this tumor.

Surgical treatment: Cautery destruction or surgical excision should be considered first and as early as possible. For small lesions, this is usually a simple matter. In certain areas, and certainly in larger growths, surgical excision may be deemed dangerous or deforming (Fig. 4).

Carbon dioxide ice freezing method: This method is widely used by dermatologists and often with excellent results. It should be used only for entirely cutaneous lesions. It is especially valuable in patients who present very spotty distributions of the growth.

Surface radiation: In our experience, surface radiation should be accomplished with radium rather than x-ray. It is most advantageous in those growths which are superficial, not necessarily being entirely cutaneous but in which the involvement is not very deep. In the deeper extensions the supplying arteries around which recurrences most often start, though in need of the most intense treatment, receive the least from surface radiation. Thus in an attempt to cure the lesion, sufficient surface radiation may be given to damage the skin with underlying active angiomatous tissues still present.

Fig. 1. a, left, Typical arterial angioma appearing during first 2 weeks of life and growing steadily until its present stage at the age of 6 months. The tip of the nose is involved with considerably more depth of tumor than is evident in the photograph. The mucous membrane of the underlying septum and the columella were also involved. Treatment was by interstitial implantation of 5 gold seeds, each containing ¼ millicurie of radon. b, This single treatment sufficed for a cure as is shown in the picture taken at the age of 5 years. There is no gross abnormality of the skin and the growth of the nasal cartilages and bone has progressed normally.

a b c

Fig. 2. a, Six months old child admitted to the hospital in critical condition due to respiratory obstruction as a result of extreme involvement of deep neck and peritracheal structures with arterial angioma. This had appeared shortly after birth and grown rapidly despite feeble efforts at control with carbon dioxide snow. The area so treated may be seen on the scalp over the parietal area. Treatment was with interstitial implantation of 35 gold seeds, each containing ½ millicurie of radon to the neck area from trachea on the left to just back of the ear on the opposite side. Within 10 days, the child was free from respiratory embarrassment. Two months later, 10 seeds, each containing ½ millicurie of radon, were implanted in the scalp, cheek and ear areas. Three months later, 10 seeds, each containing ¼ millicurie of radon, were implanted here and there about areas of activity. b and c, Result 4 years later. There is considerable scarring of the skin, principally the result of the tumor. A tight plica down the left side of the back of the neck has been released by the interdigitation of flaps. There is no evidence of angioma.

Fig. 3. a, left, Four months old infant with rapidly growing angioma originating near lower eyelid. In addition to the skin involvement, there is a marked proptosis of the eye due to direct extension of the angioma into the orbit. There is full thickness cheek involvement down to the level of the mouth slit, and some red showing on the mucosa of the cheek. b, Result 6 weeks after treatment with 40 gold seeds, each containing ¼ millicurie of radon; 12 of these were implanted into the orbit, the others in the eyelid and cheek. There is recession of the proptosed eyeball to its normal position. The area of skin involvement has faded considerably and the cheek has become less swollen. The improvement has progressed since, and no further treatment is anticipated.

Interstitial radiation: It has been found that the interstitial implantation of gold radon seeds is the most valuable single method of therapy for "malignant" arterial angiomas, which present a difficult therapeutic problem[1] and with which this paper is concerned. The factors to be considered in making this choice of treatment are as follows.

1. If there is involvement of facial features, both the hemangioma and its treatment threaten the patient with deformity or interference with function (Figs. 1, 5). Surgical removal of a growth of the eyelids, nose, or lip may sacrifice so much of the feature that reparative operations may be necessitated. Accurate surface application of radiation in these areas may be difficult or impossible, or there may be such depth of involvement that sufficient surface radiation would endanger the skin. Interstitial radiation can here be done accurately and effectively.

2. The total bulk of involvement, even though it may be on an extremity or the trunk, may prohibit surgical removal and its depth may make interstitial radiation the method of choice (Fig. 2).

3. The location may be such as to make surgery dangerous to important structures (Figs. 2, 3). This is illustrated by the moderately frequent appearance of angiomas in the 7th nerve region or with deep extensions in the neck. Interstitial radiation in these regions has been of great im-

[1]Am. J. Surg., 1938, 39: 452-457.

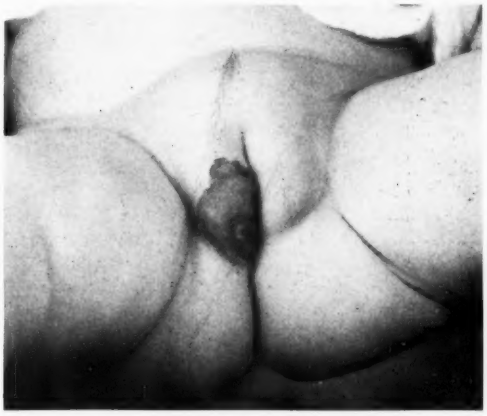

Fig. 4. Growing angioma in an infant of 5 months. The vaginal orifice is being invaded. There is spontaneous ulceration of the surface. Surgical excision would be deforming, surface radium application would be inaccurate and the deeper supplying vessels would not be adequately radiated. Treatment with 8 gold seeds, each containing ¼ millicuries of radon, produced prompt control with some temporary increase in ulceration but with minimum damage to normal structures. No further treatment is anticipated.

Fig. 5. a, left, Arterial angioma occurring on the lower eyelid of an infant and reaching its present size in 8 weeks. If uncontrolled, this could soon involve the conjunctiva and could even threaten the eye itself (see Fig. 3). Surgical excision could be done, but this would necessitate replacement of skin and would definitely have damaged the musculature of the lower eyelid. The accurate application of surface radium would be difficult as would be the treatment with carbon dioxide snow. This was treated by the interstitial implantation of 3 gold seeds, each containing ¼ millicurie of radon. b, The child is shown 6 months after treatment. This is a good result from the standpoint of selection of dosage. There has been control of the tumor without damage to the surrounding tissues and a progressive fading of the "birth-mark." It is expected that the slight discoloration of the skin still present will improve further with time.

Fig. 6. a, left, Arterial hemangioma of the rapid growing variety which is approaching the axillary structures. Spontaneous ulceration is present. Surgical removal would be difficult from the standpoint of closing the wound. This is one of our earlier cases in which radon was employed. b, The result 4 years after treatment. There was ulceration of the wound resulting in a poor cosmetic appearance in the center of the area. This is the result of improper distribution of the seeds and overradiation of the center of the wound. Treatment was with 20 gold seeds, each containing 0.5 millicurie of radon. On the basis of subsequent experience, it would have been better to have used seeds of 0.25 millicurie content, getting a more equal distribution of the seeds and repeating this treatment if necessary at any point. The dark areas are not angioma but pigmentation of the scar. Function is normal.

portance in eradicating deep growths with minimum damage to the skin and without endangering other important structures.

TECHNIQUE OF TREATMENT

Anesthesia may be general or local, depending on the size and location of the growth and the age and condition of the patient. For the introduction of the radon, which is contained in a tiny gold seed, a hollow needle fitted with a plunger for the expulsion of the seed is used. The success of the treatment depends on getting adequate and equal radiation to all portions of the growth. Multiple introducers are used, oftentimes making a separate puncture of entrance for each introducer. For a small growth, all points of deposit of the radon seeds may be reached through a single puncture. The gold seeds, containing a known amount of radon, are introduced where desired, an effort being made to estimate the point of deposit to obtain a uniform distribution of seeds, not neglecting any ramification of the tumor, and allowing an equal amount of tumor to each seed. Hemorrhage is not severe and can be controlled by a few moments of pressure, or a pressure bandage may be applied for 24 hours.

Dosage. A fairly small dosage of radiation per unit of volume of tumor is required, but this radiation should be uniform throughout the tumor, and especially the deepest ramifications must be adequately radiated. The skin and the mucous membranes should be protected from overexposure. Thus the insertion of the seed directly under either of these structures is to be avoided when possible. If this is impossible, as in the eyelid or nose of the infant, then the millicurie content of each seed must be small. The possibility of damage to the cornea or lens of the eye and to growing bone and cartilage must be constantly kept in mind (Fig. 3). Estimation of the proper dosage and the difficulty in getting uniform distribution of the seeds in the tumor are the weakest points in this plan of treatment. Caution is necessary in calculating the dosage, and it is highly desirable that overradiation be avoided even if some areas of the tumor may need a second treatment. It is desirable to gain control of the tumor with the least amount of radiation possible to get the best cosmetic result as well as to avoid damage to adjacent structures.

In treating cancer, frequently gold seeds containing 1, 1.5, or even higher millicurie content are used. In dealing with hemangiomas, most frequently seeds of 0.25 millicurie should be employed. Especially is this true about the eyes, nose, or other delicate tissues. When there is a greater volume of angioma and delicate organs are not involved, the content of each seed may be 0.50 millicurie.

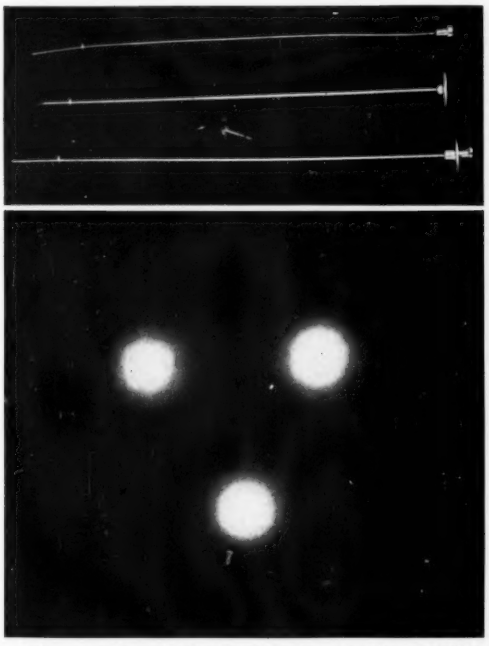

Fig. 7. a, above, Radon introducers and radon seed. The upper wire is a stylet removed from its needle directly under it. The bottom instrument is the complete introducer, the stylet being in position within the needle. The arrow points to a radon seed. This is made of gold and has walls 0.3 millimeter in thickness. Its length is 4 millimeters. b, below, Print from x-ray film exposed to 3 radon seeds 4 centimeters apart. The sphere of maximum effect of each seed is thus represented. Seeds should be implanted interstitially to allot each seed approximally this bulk of angiomatous tissue.

In general, the total dosage may be calculated as one radon seed per cubic centimeter of tissue to be radiated, the radon content of each seed to be as described previously. For flat lesions of no great depth, as can occur on the eyelid, it may be necessary to employ one seed to each square centimeter.

COMPLICATIONS

1. *Ulceration of the tumor.* In larger, rapidly growing, arterial angiomas, ulceration appears spontaneously without treatment or undue trauma in many cases (Figs. 4, 6). This indicates a lack of vitality of the tissues. Any form of treatment, with the exception of total excision, is likely to add to this ulceration before healing occurs. Infection within the tumor mass with the

formation of multiple infected thrombi is always a possibility. This has occurred in only one case. The percentage of incidence of this complication is low. It is not thought to be any higher with the use of interstitial radiation than with any other type of treatment, exclusive of the total removal of the growth.

2. *Secondary deformity.* The cosmetic result will largely depend on the amount of damage that has been done to the surface structures by the presence of the tumor itself (Fig. 2). If due caution is observed in selecting the dosage, damage to the cornea or lens, cessation of growth of nasal cartilages and bone, undue loss of subcutaneous tissue, or the development of a radiation dermatitis in later life is thought to be minimal.

3. *Recurrence.* Secondary treatment may be necessary if some portion of the tumor is not controlled at the original treatment. This may be with more interstitial radiation or in some instances combined methods are desirable. Small outlying spots may be excised or cauterized. Purely cutaneous areas may be treated by surface means.

4. *Late surgical repairs.* Surface repairs may be necessary in some instances in which the presence of the growth itself has caused poor appearance of the skin. This is true if some sloughing of the tumor has occurred, involving a feature. If the scalp is involved, excisions of bald spots may be desired.

5. *Retention of the gold seeds.* The gold seeds which contained the radon are of course retained in the tissues. There is no surrounding tissue reaction to the gold. Although the seeds are very tiny, they may occasionally be visible if placed directly under the skin of the eyelid. If so, they may later be removed.

RESPONSE TO TREATMENT

The more rapidly growing hemangioma responds more readily than does the slower growing one. Usually within a week's time there is a definite decrease in the blood flow through the tumor. A speedy recession of the growth is usually noted after 3 weeks. Ideally, progressive improvement should occur over a period of 6 months to a year in cases in which the minimum but adequate dosage has been used.

THE MECHANISM OF JAUNDICE IN CANCER OF THE PANCREAS

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THE classical picture of painless progressive jaundice with dilatation of the gall bladder, the syndrome of "pancreaticobilaire" of Bard and Pic, and again emphasized by Courvoisier, remains more of an approximation than an exact description in most cases of cancer of the head of the pancreas. More often than not, there exists some variation in the picture. Frequently there is pain (Barron, Clute, Friedenwald, Ransom); occasionally the jaundice is intermittent and sometimes there is no jaundice at all. Cancer of the body or tail of the pancreas or of both is always considered by contrast to be associated only rarely with jaundice, the syndrome "pancreatico-solaire" of Chauffard, yet cases often have been encountered in which jaundice is present (Duff). Variations in the clinical picture may occasionally be produced by complicating biliary calculi, but this is not responsible for the deviation from the classical syndrome in most cases.

NATURE OF STUDY AND INCIDENCE

The cases of cancer of the pancreas which came to autopsy at the Queens General Hospital during the 7 year period from July, 1935, to July, 1942, have been reviewed, with special consideration as to location of the primary tumor, involvement of the biliary duct structures, and the presence or absence of jaundice. Only physical factors of obstruction were considered, with no attention to biochemical mechanisms involved in jaundice. In all cases of jaundice, the biliary duct structures were carefully studied histologically to confirm involvement by tumor. The group comprised 39 cases of cancer of the pancreas. Those involving the head, with or without involvement of the rest of the organ, are considered under the general heading of cancer of the head. Those in which the head is not involved are grouped together as cancer of the body or tail or of both.

Of the 39 cases, 25, or 64 per cent, were in the head; and 14, or 36 per cent, were in the body or tail or both. Hick reports 46 per cent occurring in the body and tail, but most other series give a higher figure for head involvement. Some of the series are from surgical rather than autopsy material, so that a lower incidence for body and tail origin of the tumors would be expected (Table I).

TABLE I

		Head	Body or tail or both
Duff	Autopsy	28+3	7+10
Grauer	Autopsy	15+11+3	3
Hick	Autopsy	22+4	23
Lahey	Surgical	38+4	1
Ransom	Both	60%	30%
Queens General hospital autopsy		25	14

The age incidence ranges from 17 to 75, with an average of 58 years. There was no significant variation between the individual subgroups segregated by location or complications. The 6th and 7th decades show the highest incidence, with 11 in each, or a total of 56 per cent, occurring in the 20 year period between 50 and 70 years of age. The sex incidence showed marked preponderance of males, a ratio of 26 to 13, or 2 to 1. This is well recognized, and was noted in all but one of the series reviewed in the literature (Barron, Duff, Franco, MacKinnon, Ransom, 23).

CLINICAL AND PATHOLOGICAL DATA

The clinical picture showed marked variation. Weight loss, anorexia, and weakness were the most constant findings. Pain was present in 12, and noted as being absent in 8 cases of cancer of the head. It was present in 11 and absent in 3 cases of cancer of the body or tail or of both.

Of the 39 cases, 19 showed jaundice, and this represents the group selected for study in this presentation. Of the 25 cases of cancer of the head, 13 presented jaundice, including 1 case in which it was intermittent. Six of the 14 cases of cancer of the body or tail or of both had jaundice. In a comparable series, Duff lists 13 or 16 cases of carcinoma of the head, and 8 of 16 cases of carcinoma of the body or tail or of both, with icterus. He makes the point that jaundice is a much later manifestation in the cases originating in the body or tail or of both, often appearing only terminally. This was not borne out by the present series. With the exception of 2 cases originating in the head

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Fig. 1. Direct extension of cancer of head of pancreas to common bile duct with annular stenosis and obstruction.

Fig. 2. Direct extension of cancer of head of pancreas to common bile duct with annular stenosis and obstruction.

and surviving 5 to 7 months respectively after the appearance of icterus, the duration of jaundice was comparable in both groups. Excluding these 2 cases, the average duration of jaundice was 5 weeks in both groups. It ranged from 1 to 9 weeks in the group arising in the body and tail, and 2 to 9 weeks in the group with the primary tumor in the head.

When jaundice was present, the correct diagnosis was made clinically before operation or autopsy in 5 cases, and was considered a possible diagnosis in 5 additional cases of cancer of the head, and in 1 case of cancer of the body and tail. However, in the absence of jaundice, the diagnosis of cancer of the pancreas was almost invariably missed in this, as in other series (Haines, Adams Duff). The reason for the difficulty in diagnosis of these cases is readily understandable. The primary tumor, whether located in the head or body or tail, does not of itself produce symptoms. The neoplasm is deeply placed and is undetectable by ordinary means of external or internal examination. It is only when the biliary tract is affected secondarily that recognizable symptomatology usually appears. When this involvement of the biliary ducts does not occur, then ordinarily it is the spread of the tumor that leads to its detection. The first symptoms are then usually referable to some other part of the gastrointestinal tract, to some distant metastasis, or to the generalized carcinomatosis. Cancer of the pancreas is one of the most common latent forms of malignant tumor.

Cancer of the pancreas spreads by direct extension, by lymphatics, by blood stream, and by peritoneal implantation. Direct spread may lead to invasion of neighboring hollow organs and the spleen. There was invasion of the stomach in 6 of our cases, of the duodenum in 9, and of the transverse colon in 2. Obstruction of the gastrointestinal tract followed in 5 instances, and ulceration and hemorrhage occurred in 6 cases. The bleeding in the latter group occurred usually into the gastrointestinal tract, but in 2 cases it was into the peritoneal cavity. Lymphatic spread led to

invariable involvement of the regional lymph nodes and often further involvement of the retroperitoneal, periaortic, hypogastric, mesenteric, and mediastinal nodes. Hematogenous spread led to the involvement of the liver in 25 cases, the lungs in 10, the kidney in 3, the adrenal in 5, and the ovary in 1 case. The figures for brain and bone metastasis are incomplete. The liver may be reached by lymphatic as well as hematogenous routes and the resulting occasional picture of widespread lymphatic permeation about the duct structures is rather characteristic of pancreatic tumor origin. In most instances, the liver metastases were small, but in 2 cases they were massive. Peritoneal carcinomatosis was present in 12 of the cases.

Duff claims that cancer of the body and tail are more apt to give rise to widespread metastatases because of anatomic factors which facilitate the spread from this region; i.e., the more extensive peritoneal surface, the more generous lymphatic supply, particularly the lymphatics along the nerve bundles of the celiac plexus, and the presence of the large splenic vein as an avenue for hematogenous spread. This explanation seems hardly necessary in view of the fact that cancer of the body and tail produces a biliary obstruction less often, which complication is apt to lead to the death of the patient before widespread dissemination has had a chance to take place.

Pancreatic tumors may be of duct, acinar or islet tissue origin. In this series, the histology of the tumor suggested duct origin in 24 instances, acinar in 13, and both types of histological structure were present in 2 cases. The cases which produced jaundice showed a higher percentage of duct adenocarcinoma than those in which there was no jaundice present. Scirrhous reaction was noted in all but one of the adenocarcinomas, whereas the tumors suggesting acinar origin were uniformly more medullary. Various degrees of differentiation were found, varying from well oriented glandular structure to extreme anaplasia, suggesting sarcoma.

The size of the primary sites showed marked variation. The actual dimensions are not included in this study. Difficulty in judging exact size of some of the larger tumors was encountered because of the merging of metastatic nodes with primary tumor mass and regional extension. In general, the acinar tumors were larger and more medullary. In 1 case, the primary tumor measured 1.5 by 1 centimeter on cross section. By involving the adjacent duct over a narrow segment, this tumor lead to the classical picture of painless progressive jaundice over several weeks' duration.

Fig. 3. Direct extension of cancer of head of pancreas to common bile duct with annular stenosis and obstruction.

The patient survived a cholecystoduodenostomy by only a few days, but at autopsy the lesion was distinctly operable. It is regrettable that the primary tumor was not found at the exploratory exposure and a resection of the head of the pancreas attempted. It is this type of lesion which offers the best prognosis for permanent cure by surgery, inasmuch as the symptoms appear before metastasis renders the lesion inoperable. In general, the tumors of the head of the pancreas were smaller. All neoplasms of the body or tail were obviously inoperable with metastasis present at the time of autopsy.

ANALYSIS OF MECHANISM OF OBSTRUCTION

It is commonly taken for granted that jaundice in cancer of the head of the pancreas is due to "extraductal" compression of the common bile

Fig. 4. Photomicrograph of section of a cancer of the head of the pancreas with bulky papillary extension to duct with filling of lumen.

duct, for widespread liver metastasis is exceptional (Courvoisier, Adler, Duff, Lockwood). Jaundice in cases of cancer of the body, the tail or both body and tail is likewise usually explained by compression of the biliary tract by metastatic lymph nodes in the region of the porta hepatis. Whereas it might be understandable that a growing mass in a fixed organ like the pancreas might cause compression of the ducts, enlarging lymph nodes at the porta hepatis do have room for expansion and should not cause obstruction unless they are fixed to the duct wall to the surrounding structures or to both. Such fixation of bile duct structures by tumor was invariably found in our cases. Cancer was present not only in the lymph nodes along the biliary tract, but was also present in the wall of the duct itself. Likewise, passive compression alone of the common duct within the head of the pancreas proper is not borne out by our experience. There was cancerous invasion of the biliary duct wall in all cases of cancer of the head with jaundice (Figs. 1, 2, 3). In the 19 cases with obstructive jaundice, 18 showed on microscopic study, histological invasion of the wall by tumor tissue. In the sole remaining specimen, the gross involvement of the duct wall was obvious It is therefore believed that malignant involvement of some part of the biliary tract is a prerequisite for the production of the biliary obstruction responsible for the jaundice associated with cancer of the pancreas.

The observation of several large cancers of the pancreas some 10 years ago, and also of a large pancreatic cyst, which displaced and distorted the common duct markedly, with obvious flattening and compression of the lumen and, nevertheless, *failed* to give any evidence of jaundice or other evidence of obstruction, seemed to give added weight and significance to our observations. Since that time, every case that has shown definite obstruction with persistent jaundice has invariably shown to some degree, *invasion of the duct wall by tumor tissue.*

From the primary tumors of the head of the pancreas, the common bile duct was involved in 12 of the 13 cases with obstruction. In 9, the intrapancreatic portion was invaded by direct extension from the primary tumor. In 3, the extrapancreatic portion, just below the junction of the cystic and hepatic ducts, was involved by extension from metastatic carcinomatous lymph nodes. In only 1 case was the extrahepatic biliary tract found free. This was 1 of the 2 cases with massive liver metastasis, in which the intrahepatic ducts near the hilus were definitely invaded. Gallbladder enlargement was present in 9 cases, one of which also showed calculi. The 3 cases without enlarged gall bladders showed evidence of fibrosis or chronic cholecystitis and cholelithiasis, and this was deemed adequate to explain the failure of dilatation.

In the cases of cancer of the body or tail or of both, the upper extrapancreatic portion of the common bile duct was invaded in 3 cases, all of which showed gall bladder enlargement. In 2 cases the common hepatic duct was involved, and in 1 both the right and left hepatic ducts were involved. The latter case is particularly pertinent for the consideration of the mechanism we are stressing. In this last case, the left hepatic duct was more completely occluded than the right duct, and, corresponding to the degree of stenosing obstruction, the left lobe of the liver showed deeper bile staining than the right. As would be expected, there was no enlargement of the gall bladder when the obstruction was above the cystic duct.

The infiltrating cancer was in some cases limited to the outer layers of the duct wall, but in most

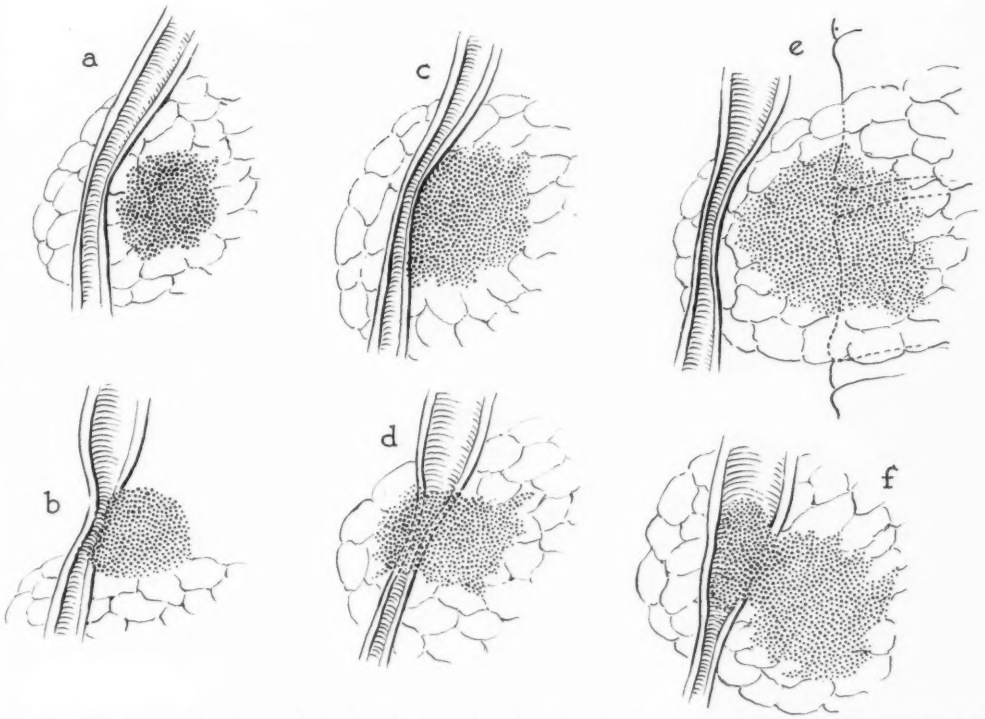

Fig. 5. Diagrammatic representations of mechanisms of obstruction of duct by cancer. *a*, Tumor mass in head of pancreas displacing but not obstructing lumen of duct. *b*, Tumor mass just above pancreas, possibly lymph node, extending to wall with local annular stenosing scirrhous reaction causing obstruction of relentless progressive character. Detailed diagram seen in Figure 6. *c*, Tumor in head of pancreas extending to wall of duct, fixing and displacing same, with some narrowing of lumen. It is obvious that progressive growth of tumor as a whole leads to further direct impingement upon lumen. *d*, Tumor of head of pancreas with extension to duct wall and mechanism of annular stenosis and tumor extension both operative in producing obstruction. *e*, Tumor of pancreas which is fixed to vertebral bodies which also displaces the duct, with kinking and narrowing of lumen. *f*, Tumor of head of pancreas without scirrhous reaction with medullary tumor extension into lumen often associated with intermittent jaundice brought on by repeated sloughing of interluminary tumor extension.

cases the mucosa was also involved, with secondary ulceration. In one case there was polypoid extension of the tumor into the lumen (Fig. 4). Secondary necrosis and sloughing of this growth allowed regression of the jaundice as is frequently seen in primary tumors of the ampulla, biliary tract proper, or stone in the duct. Invasion of the intrahepatic and extrahepatic biliary ducts as a factor in the production of jaundice in cancer of the pancreas has been mentioned by several authors, but its constant presence in these cases has not been stressed.

DISCUSSION OF MECHANISM

There are three separate factors in the production of the obstruction of the biliary tract in this series (Fig. 5). First, *invasion fixes* the wall of the duct and permits of physical compression with narrowing of the lumen in lieu of mere displacement by adjacent expanding tumor mass. Second, and this is the more common and more important mechanism in our experience, the invasion of the duct wall is accompanied by a scirrhous reaction with the production of an annular *stenosing* lesion with localized segmental narrowing and obstruction of the lumen (Fig. 6). This occasions the classical syndrome of "pancreatico-bilaire" more often. A small resectable tumor or a localized area of extension from a metastatic lymph node to the duct can produce this classical picture. Finally, the invasion of the duct wall may be associated with extension to, and *filling* of, the

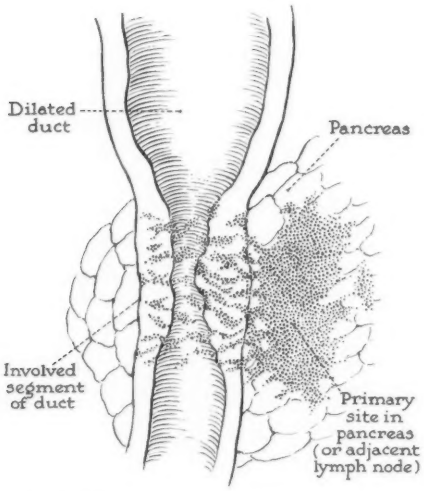

Fig. 6. Diagrammatic representation of the most common mechanism of obstruction from primary site in pancreas or adjacent lymph node. As would be expected this scirrhous annular progressive constriction is seen in scirrhous tumors of the pancreas, the most common form.

lumen with tumor tissue with obstruction of the flow of bile. This last lesion is often associated with a cellular medullary or papillary type of growth and by sloughing may give periods of spontaneous remission of jaundice.

An identical mechanism, i.e., metastases to lymph nodes and then extension to biliary tract, was found to account for the jaundice in cases of primary cancer of the stomach and colon, which did not have extensive liver metastases. In several such instances, there were found metastases to the lymph nodes at the porta hepatis with secondary invasion of the bile ducts. The fact that massive liver metastases with very little remaining liver parenchyma is often unassociated with jaundice, lends significance to the smaller nodules involving the intrahepatic ducts near the hilus for the production of the icterus. This suggests that in cases of massive liver metastasis also, duct invasion may be a prerequisite for jaundice.

SUMMARY AND CONCLUSION

Thirty-nine cases of cancer of the pancreas have been reviewed. Nineteen cases showed the presence of jaundice, 13 originating from the head, and 6 from the body or tail. There was carcinomatous invasion of some part of the biliary tract in all cases with jaundice. Obstruction by compression alone was not encountered. Some degree of fixation of the duct seems necessary for effective obstruction by mechanical compression by adjacent tumor.

Obstruction leading to the syndrome of painless progressive jaundice is most often due to local stenosing annular scirrhous carcinomatous involvement of duct wall. Occasionally there is papillary extension into the lumen, in which cases sloughing may produce intermittent, or waxing and waning jaundice.

This mechanism of jaundice also applies to jaundice in cases of metastases from other foci, when involvement of the extrahepatic ducts or the larger intrahepatic ducts deep in the liver or at the hilus may become the pertinent mechanism.

The theoretical basis for cure by a resection of the head of the pancreas in early cases of cancer of the pancreas despite an advanced syndrome of progressive jaundice is implied. The known evolution of the syndrome of painless progressive jaundice occasionally by stone in the duct, is a further indication for early laparotomy in all cases of persistent jaundice.

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WOUND IMMUNITY

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IN a previous communication (3) we described experiments on guinea pigs and dogs which were designed to ascertain the normal rate of wound healing and the reactions of fresh wounds to contamination with Staphylococcus aureus. The following experiments were performed for the purpose of determining the length of time required to establish local immunity in incised wounds and the anatomical extent of such immunity.

As in previous experiments the abdominal walls of guinea pigs were shaved, cleaned with soap and water, and antisepticized with tincture of merthiolate. Aseptic technique was used and all operations were performed under ether anesthesia. An incision 5 centimeters long was made in the abdominal wall extending through the skin, subcutaneous tissue, and abdominal muscles. Incisions were closed with interrupted silk sutures in the muscle layers, subcutaneous tissue, and skin. No bandages were applied, and the guinea pigs were returned to their clean cages immediately after operation. A culture of Staphylococcus aureus was obtained from a patient with a carbuncle. The organism was grown 6 hours upon chopped meat medium, transferred every 24 hours, and occasionally plated on blood agar to check for purity. Virulence of the organism was determined by injecting the culture subcutaneously in guinea pigs.

INOCULATION OF HEALING WOUNDS WITH STAPHYLOCOCCUS AUREUS

Following the technique of Du Mortier we saturated a small sterile cotton swab with a sufficient amount of culture to produce infections in incisions made 12 hours before. The smallest amount which uniformly produced such infection was 0.8 cubic centimeter. In the first group of guinea pigs the culture was rubbed vigorously on the wound 2 hours after the conclusion of the operation. There was no way of determining how much culture was introduced into the wound, but our interest was in the resistance of surgical wounds to outside contamination. Eight pigs were used and all developed wound infections. The results were checked by microscopic examination.

Similar experiments were performed on different groups of guinea pigs which were inoculated at the end of 12 and 24 hours. All wounds became infected within 2 to 4 days after inoculation, 2 pigs died and 2 developed large abscesses in the abdominal wall. Fifty per cent of the guinea pigs inoculated at the end of 48 hours and 20 per cent of those inoculated at the end of 72 hours developed infections. None was infected by cultures rubbed on the wound 96, 120, and 144 hours after operation. Leucocyte counts were recorded for 3 days prior to each experiment and each day thereafter during the experiment.

In order to check for possible variation of culture virulence, guinea pigs were operated on each day on 6 successive days and then the culture was applied to all of the wounds on the last day. The results were the same as in the previous experiments.

Our conclusions were that on the 4th day an immunity or change occurs which protects the incision from infection by Staphylococcus aureus when it is rubbed on the wound. A leucocytosis was observed after inoculation in practically all animals which had been operated upon 2, 12, and 24 hours previously; a lesser response was observed at 48 and 72 hours. Inoculation after the 4th postoperative day produced no important variations in the leucocyte counts (Fig. 1). This finding leads us to believe that after the 4th postoperative day local immunity is so great that absorption does not occur unless trauma is inflicted to the granulation tissue.

From the Department of Surgery, Indiana University School of Medicine, Indianapolis, Indiana, in co-operation with the Department of Bacteriology. This study was aided by a grant from the Eli Lilly Research Fund.

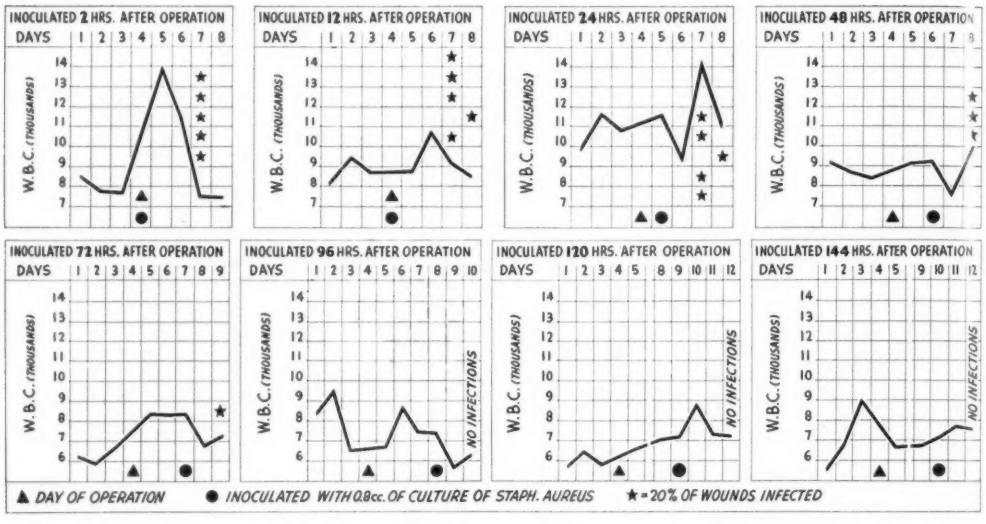
INOCULATED 2 HRS. AFTER OPERATION
INOCULATED 12 HRS. AFTER OPERATION
INOCULATED 24 HRS. AFTER OPERATION
INOCULATED 48 HRS. AFTER OPERATION
INOCULATED 72 HRS. AFTER OPERATION
INOCULATED 96 HRS. AFTER OPERATION
INOCULATED 120 HRS. AFTER OPERATION
INOCULATED 144 HRS. AFTER OPERATION
DAYS
W.B.C. (THOUSANDS)
NO INFECTIONS
▲ DAY OF OPERATION
● INOCULATED WITH 0.8cc. OF CULTURE OF STAPH. AUREUS
★ = 20% OF WOUNDS INFECTED

Fig. 1. The leucocyte response following inoculation of an abdominal incision with 0.8 cubic centimeter of a culture of Staphylococcus aureus. The graphs were prepared by summarizing a series of experiments. Each star indicates 20 per cent of infected wounds and they are placed on the day on which the infections occurred after inoculation.

EFFECT OF INOCULATION OF HEALING WOUNDS AFTER REMOVAL OF STITCHES

Fourteen guinea pigs were operated on as previously described. Stitches were removed from incisions made 12, 24, 48, 72, 96, 120, and 144 hours previously. In each instance 0.8 cubic centimeter of a 6 hour culture of Staphylococcus aureus was rubbed on the wound with a sterile cotton swab immediately after removal of the stitches. The experiments were then repeated on 14 more guinea pigs to check the virulence of the culture. Incisions were made 12 to 144 hours before, all stitches removed and wounds inoculated the same day.

The results in both groups were the same. All wounds were infected which had been made 12 and 24 hours previously. Eighty per cent of 48 hour wounds were infected, 50 per cent of 72 hour wounds were infected, 20 per cent of 96 hour wounds were infected, and none were infected at 120 and 144 hours.

ANATOMICAL EXTENT OF LOCAL IMMUNITY

A group of experiments was now done to determine whether wound immunity is due to local or systemic factors or both; and to learn how wide an area is protected by the regional immunity.

A left paramedian abdominal incision was made and sutured as described in previous experiments but no organisms were purposely introduced. At the conclusion of the operation a right paramedian incision was made and 0.3 cubic centimeter of a 6 hour culture of Staphylococcus aureus was introduced in the second incision. The second incision was made in other guinea pigs at the end of 12, 24, 48, 72, 96, 120, and 144 hours after the first incision. In each instance the culture was introduced at the time of the second operation into the second wound. The wounds were closed with interrupted silk sutures. Each experiment was repeated 4 times varying the site of the second incision in the abdominal wall.

The entire experiment was then repeated; 12 guinea pigs were used and 2 of them were operated upon on each of 6 successive days. On the 6th day the second incisions were made in various sites of the abdomen, 0.3 cubic centimeter of the culture being introduced in each second incision on the same day, thus eliminating variation in the virulence of the culture.

In a third group the first incision was reopened at the time that the second incision was made and the culture was introduced in both wounds.

Infections occurred in all second incisions made immediately after the first and inoculated, also in all incisions made 12, 24, and 48 hours later. Eighty per cent of the second incisions were infected when made and inoculated 72 hours after operation and 50 per cent when made and inoculated 96, 120, and 144 hours later.

In the third group the first incision behaved very much as in previous experiments except that immunity was not established until 144 hours after operation. All second incisions were infected when made and inoculated 12, 24, and 48 hours after the first. Fifty per cent of second incisions made after 96 hours and inoculated became infected.

ANALYSIS OF RESULTS

Du Mortier found that 56 per cent of his guinea pigs became infected when Staphylococcus aureus was implanted 2 days after operation, and that complete immunity did not occur until the 5th day. Since our pigs were not restrained it is reasonable to suppose that respiration, circulation, and hydration were normal. These factors together with the omission of bandages may have hastened local immunity in our animals. This is further substantiated by the fact that local immunity did not occur until the 6th day when 2 incisions were made at different times. The second incision may have delayed the process of immunity.

It is interesting to note that 100 per cent of the pigs were infected when Staphylococcus aureus was rubbed on the wound at the end of 2, 12, and 24 hours, whereas previous studies (3) revealed that only 67.5 per cent were infected when the culture was introduced into the wound at time of operation. This is in accord with clinical experience, for Koch and others have shown that most wounds although primarily contaminated are more often infected later when treated without strict asepsis. We cannot say what rôle the vigorous rubbing played but it undoubtedly added trauma and destruction of some cells although the scabs were not rubbed off by the process. On the 3d day only 20 per cent became infected, and none were infected on the 4th, 5th, or 6th days.

When stitches are removed immunity does not occur as early. Wounds were not immune until the 5th day whereas the former groups were immune on the 4th day. But in the process of removing stitches more trauma is inflicted. Scabs were removed and bleeding occasionally occurred.

Previous incisions made in the abdominal wall do not protect fresh incisions against staphylococcic infections. Local immunity is apparently limited to the zone of granulation tissue and does not extend beyond this zone. In this way it corresponds to the pyogenic membrane or leucocytic barrier referred to in localized infections. However, on the 4th day following a previous incision and thereafter as long as the experiments were continued only 50 per cent of second incisions became infected. This would indicate some degree of regional and general immunity. Temperatures and leucocyte counts tend to bear out the latter as shown by our previous studies.

When the first wound was reopened and inoculated, immunity did not occur until 6 days in contrast to 5 days when stitches were removed and 4 days when the culture was rubbed on the undisturbed wound. At 6 days the second wounds were infected in 50 per cent of the animals although the old incisions were immune.

This observation indicates that any trauma to granulation tissue delays the onset of local immunity; also systemic and local disturbances such as infected second wounds may cause the delay. Previous studies showed an incidence of infection in 67.5 per cent when cultures are introduced in a freshly made incision. We have shown that when a second wound is made immediately after the first or when made 12, 24, or 48 hours later, 100 per cent of these second wounds become infected. We may therefore deduce that there is a decrease in regional resistance over the entire abdominal wall for a period of 48 hours. On the 4th day there is an increase in resistance and only 50 per cent of second wounds are infected. Similar results were obtained by

scrubbing the abdomen (1) without the previous incisions, a fact indicating that the increased resistance may be due to the reaction caused by the trauma of scrubbing or of the incision. A great increase in blood supply was noted at the time of all second incisions. This evidently was only one of the factors involved in increasing local resistance.

Lastly, the behavior of the first wound varied slightly in the presence of a second one. That is, immunity was delayed but was none the less complete. This was probably due to the increased trauma of reopening the wound. But the complete immunity which occurred on the 6th day further corroborated previous observations that the area of immunity is limited to the zone of granulation tissue.

OBSERVATIONS

Our experiments show that a wound is about 33 per cent more susceptible to infection during the first 24 hours than it is at the time it is inflicted. We have always believed that if a wound can be carefully scrubbed with soap and water during the first 6 hours it could probably be rendered sufficiently sterile to permit healing by first intention. This result occurs if the scrubbing can be done under strict aseptic technique. In combat zones it is probably better not to attempt sterilization, but merely to ligate major bleeding vessels and apply a sterile pressure bandage to burned and traumatized areas. This procedure limits the loss of blood and plasma into the injured area, thereby reducing the incidence of shock and infection (2). Above all, however, it prevents the possible introduction of bacteria into a more susceptible wound. If a clean-up process together with removal of foreign bodies or final reduction of a compound fracture is to be done, it is preferable after the 6th day. Sulfonamides given by mouth or parenterally at the time of injury will reach the wounds and blisters during their exudative phase. Since the wounds treated by this method are not sutured, anaerobic infections are less apt to occur. In addition tetanus toxoid and polyvalent gas gangrene antitoxin should be used. Should infection occur bandages must be removed and the areas treated as open infected wounds.

Surgeons have long ago learned not to enter the abdomen through a gunshot wound. An incision is made depending on the site of entrance and exit of the bullet. The bullet wound is excised or unmolested—the rationale for the latter procedure is clearly demonstrated by our experiments.

CONCLUSIONS

1. Healing wounds are more susceptible to contamination by Staphylococcus aureus during the first 24 hours than are fresh wounds.
2. Immunity in a healing incision which is not traumatized occurs 4 days after surgery.
3. When sutures are removed from a healing wound, immunity does not occur until the 5th day after operation.
4. If the wound is reopened this immunity does not occur until the 6th day, due probably to the trauma incurred in reopening.
5. The anatomical extent of wound immunity seems to be limited to the area surrounded by granulation tissue.
6. The entire abdominal wall around a previous incision is less susceptible to staphylococcus implantation after the 4th postoperative day.

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THE SURGICAL MANAGEMENT OF PROLAPSE OF THE UTERUS AND VAGINA

A Report of 730 Personal Operations

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UTEROVAGINAL prolapse is one of the commonest lesions encountered in the practice of gynecology. While the disorder in itself is not responsible for the loss of human life, it is the cause of untold discomfort and suffering. In approaching this problem from the surgical standpoint, it must be borne in mind that since *a priori* uterovaginal displacement does not cause death, the method employed for the correction, in order to justify itself, must have a very low operative mortality. Because of the multiplicity of complicating lesions associated with uterovaginal prolapse, it is obvious that no one operative procedure can be applied in all cases and that the best operative results will be obtained by individualizing.

My interest in this lesion covers a period of 27 years, during which time I have employed practically all the standard procedures and have tried to estimate their value impartially. During these years I have performed 730 operations for prolapse of the uterus and vagina, the data concerning which are given in tables.

Five factors are fundamental in determining the method of treatment: first, the age of the patient; second, the possibility of future pregnancies; third, the extent of the prolapse; fourth, the size of the uterus; and fifth, whether or not coexisting disease is present. For practical purposes uterovaginal prolapse may be classified in three degrees: first degree prolapse, when the cervix appears at the vulva; second degree prolapse, when the cervix is extruded; and third degree prolapse, or procidentia, when the entire uterus is found outside of the vulva.

TYPES OF OPERATION

Vaginal plastics and abdominal suspension or fixation of the uterus. In this group there were 117 cases.

It is conceded by most gynecologists that with few exceptions young women in the childbearing age should be treated conservatively, whenever possible, until their families are completed, at which time they may be subjected to corrective operations for their displacements, vaginal or uterine. During this stage of observation the cervix is the one organ that usually needs attention since, accompanying most prolapses, a laceration of the cervix with ectropion and erosion is a prevalent finding. If it is found advisable to postpone operation, the cervix should meanwhile be healed by cauterization or conization after each pregnancy. This accomplishes two purposes: it relieves the patient of an annoying discharge, and it may serve as a prophylactic measure against the development of cancer of the cervix. To put it another way, all irritative lesions of the cervix uteri should be healed between pregnancies in order to reduce the incidence of cancer. The discomfort occasioned by the lesser degrees of prolapse may be relieved by the wearing of a well fitted pessary. Those young women who have extensive prolapse should be operated upon. The operative procedures in the younger group of patients are fairly well standardized and consist of repair of the cervix by trachelorrhaphy, as well as repair of the anterior and posterior vaginal walls and of the perineum. By means of a laparotomy, the uterosacral ligaments are shortened in order to bring the cervix to its normal position and at a right angle with the vagina, and the uterus is suspended by the round ligaments. This form of reconstruction restores the pelvic organs as nearly as possible to their original state, and, in my experience, has not interfered with subsequent pregnancies and labors. In order to obviate relaxation and laceration of the repaired perineum, an episiotomy is generally performed at a subsequent delivery. High amputation of the cervix and fixation of the uterus to the anterior abdominal wall are avoided during the childbearing age, because they predispose to sterility, abortion, and miscarriage and because of the severe dystocia that these procedures will obviously cause during later labors. In women past the menopause amputation of the cervix and fixation of the uterus are employed if, for one

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TABLE I.—AGES IN YEARS

	20–24	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	Total
Vaginal plastics and abdominal suspension or fixation of uterus	5	17	28	26	20	7			1					117*
Interposition of uterus	Below 45 years		55			37	42	31	29	19	9	1	1	224
Vaginal hysterectomy with interposition of broad ligaments				6	9	12	24	20	29	17	8			125
Vaginal hysterectomy clamp method	1				2	2	2	11	6	10	1	1		36
High vaginal fixation of uterus			4	9	8	8	11	8	5	3	1			57
Manchester operation (Fothergill operation)		1	4	14	14	13	13	12	8	5	1			85
Subtotal colpectomy (LeFort operation)						3	3	6	3	5	5	1		26
Total colpectomy								3	3					6
Operation for posterior vaginal enterocele				4	8	5	8	9	9	7	3	1		54

*Includes 13 in which age was not recorded.

reason or another, it is deemed advisable to treat a particular patient by the combined method of vaginal plastics and laparotomy. When dealing with these women and with old women, one of the vaginal methods is usually selected, a laparotomy being performed only under rare circumstances. There are two reasons for this, the first being that vaginal operations increase the operability rate on account of the lessened morbidity and mortality and the second that in these women in whom childbearing is no longer a consideration, the uterus or the broad ligaments may be employed to construct supports for elevating the prolapsed uterus and bladder in the pelvis if the uterus is retained, and the prolapsed bladder if the uterus is sacrificed. An adequate repair of the pelvic floor is a complement to all prolapse operations except in the rare case of a patient with nulliparous prolapse when the perineum is intact and gives good support.

Interposition operation. The interposition operation (Watkins-Schauta-Wertheim) has been used extensively both in Europe and America in the correction of uterovaginal prolapse. I have found it a satisfactory means of treating this lesion. In our series there were 224 cases. Experience, however, has taught me that it should not be employed in the presence of a markedly atrophied uterus. The bladder, by its greater weight, aided by intra-abdominal pressure, will in the course of

TABLE II.—MAIN DIAGNOSES

	Large cystocele	Descensus uteri	Prolapse			Nullipa-rous prolapse	Recurrent prolapse	Inversion of vagina	Posterior vaginal enterocele	Total
			1°	2°	3°					
Vaginal plastics and abdominal suspension or fixation of uterus	2	43	33	20	14		5			117
Interposition operation	13	3	26	31	145	1	5			224
Vaginal hysterectomy with interposition of broad ligaments		14	11	35	46	4	15			125
Vaginal hysterectomy clamp method	1	9	1	8	13	4				36
High vaginal fixation of uterus	12	2	11	15	4		13			57
Manchester operation (Fothergill operation)	12	9	18	29	10	1	4	2		85
Subtotal colpectomy (LeFort operation)					11	2	3	10		26
Total colpectomy					2		1	2	1	6
Operation for posterior vaginal enterocele									54	54

TABLE III.—ADDITIONAL DIAGNOSIS[1,2]

Myomas of the uterus	41
Epidermoid carcinoma of cervix	1
Adenocarcinoma of corpus	3
Senile atrophic uterus	57
Cervical polypi	17
Previous abdominal fixation of uterus	5
Fibrosis of the uterus; menometrorrhagia	7
Myoma of anterior vaginal wall	1
Cyst of perineum	2
Third degree laceration of perineum	15
Rectovaginal fistula	2
Ulcer of vagina	8
Laceration of right labium minus	12
Laceration of left labium minus	1
Edema of vaginal walls	1
Vesical calculus	1
Urethrocele	3
Urethral caruncle	5
Old suburethral abscess	1
Urethral prolapse	4
Hypertrophied suburethral fold	11
Ovarian myoma	1
Ovarian cyst, left	3
Ovarian cyst, right	1
Cystic ovaries	4
Calcified tumor of right ovary	1
Perisalpingo-oophoritis	1
Rectal prolapse	4
Hemorrhoids	38
Cholelithiasis	4
Lipoma right thigh	1
Umbilical hernia	1
Inguinal hernia, right	1
Inguinal hernia, left	1
Diabetes	13
Previous vaginal operation for prolapse	22
Previous vaginal plastics and suspension or fixation	45
Old pelvic hematocele	1
Ankylosis both knees	1
Chronic appendicitis	13
Relaxed vesical sphincter	4
Endometriosis	4
Megalocolon	1
Ruptured corpus luteum with hemorrhage	1
Incarcerated femoral hernia	1
Fundal polyps	3
Incisional hernia	3
Perineovaginal fistula	1
Varicose veins (severe)	1
Lipoma of left buttock	1

[1]Cervical pathology in the form of erosion, laceration, ectropion, ulceration and hypertrophy was found in all cases except those of nulliparous prolapse.

[2]In the above table urethroceles are said to have occurred three times. A word of explanation may be necessary. In all cases of cystocele associated with prolapse, there is found a certain amount of bulging of the posterior urethral wall and some relaxation of the vesical sphincter. In all operations for cystocele this has been corrected by plicating the musculofascial tissues on the sides of the bladder in one or two layers as indicated, thus overcoming the bulging in the posterior urethral wall. The three urethroceles mentioned in the table are those in which the posterior wall formed a large hernial sac.

TABLE IV.—ADDITIONAL OPERATIONS[1,2]

Myomectomy or hysterectomy (vaginal or abdominal)	41
Vaginal hysterectomy for epidermoid carcinoma of cervix	1
Vaginal hysterectomy for adenocarcinoma of corpus	3
Cervical polypectomy	17
Myomectomy for myoma of anterior vaginal wall	1
Resection of cyst of perineum	2
Perineorrhaphy for complete laceration of perineum	15
Repair of rectovaginal fistula	2
Repair of right labium minus	2
Repair of left labium minus	1
Extraction of vesical calculus	1
Repair of urethrocele	3
Fulguration of urethral caruncle	5
Excision of abscess, wall of urethra	1
Fulguration for urethral prolapse	4
Resection of hypertrophied suburethral fold	11
Ablation of ovarian tumors	6
Puncture of cystic follicles	4
Operation for rectal prolapse	4
Hemorrhoidectomy	38
Excision of lipoma of right thigh	1
Umbilical herniotomy	1
Inguinal herniotomy	2
Appendectomy	13
Plication of vesical sphincter	4
Femoral herniotomy	1
Incisional herniotomy	3
Repair of perineovaginal fistula	1
Excision of lipoma of left buttock	1

[1]Cervical repair in the form of amputation, trachelorrhaphy and cauterization was performed in all patients in whom the uterus was retained.

[2]Under "Plication of Vesical Sphincter" 4 cases are mentioned. In all cases of cystocele, when the musculofascial tissues are plicated the vesical sphincter is also repaired. The 4 cases mentioned in the table were extreme cases, in which additional operative procedures were necessary.

time force down such an atrophied interposed uterus so that the cervix appears at the vaginal introitus, although there may be no recurrence of the cystocele. It has been shown that severe vesical disturbances may follow the interposition operation. Obviously vesical pain will occur whenever the uterus is pulled between the bladder pillars and the uterine fundus is attached to the anterior vaginal wall, since the fundus of the uterus under such conditions will exert a constant pull on the bladder and will cause its sacculation. Bladder symptoms, however, are infrequent if the bladder pillars are severed and the bladder is completely separated from its attachments to the vagina and uterus. It will then lie smoothly and not in folds, on the superior and posterior surfaces of the uterus, and, since there is no traction on this viscus, pain will not be experienced. In the interposition operation, as well as in all methods in which the uterus is retained in the management of uterovaginal prolapse, recurrences can be more easily corrected by having the uterus to work with than when it has been removed.

Vaginal hysterectomy with interposition of the broad ligaments. There were 125 cases in our series.

Vaginal hysterectomy for prolapse is valuable when the uterus shows marked senile atrophy and when because of certain pathological conditions its removal is thought to be in the patient's interest. In performing this operation I have found

TABLE V.—OPERATION FOR POSTERIOR VAGINAL ENTEROCELE

Vaginal resection of cul-de-sac of Douglas, Ward operation	41
Abdominal obliteration of cul-de-sac of Douglas, Moschcowitz type of operation	10
Total colpectomy	1
Subtotal colpectomy—LeFort operation	2
Total	54

it advantageous to ligate the broad ligaments in three sections, the lowermost section including the uterosacral ligament on each side. The broad ligaments are approximated in the median line by tying together the three sutures of each side. The cul-de-sac of Douglas is closed by approximating the uterosacral ligaments in their entire length by means of interrupted sutures. The united broad ligaments are then attached to the anterior vaginal wall, after resection of the vaginal flap of each side, by means of similar sutures. This method of approximating the broad ligaments is responsible for tying the vessels more securely and causing less tension than occurs with a continuous mattress suture, as recommended in the original Mayo operation. The closure of the cul-de-sac of Douglas is one of the most important steps of the operation, since this procedure may be the means of preventing the formation of a future posterior vaginal enterocele.

Vaginal hysterectomy—clamp method. In this group there were 36 cases.

Vaginal hysterectomy by the clamp method, as elaborated by Joseph Price and popularized by James W. Kennedy, has two distinct advantages: the rapidity with which it may be performed and its excellent results. When performed for prolapse it is profitably carried out in two steps. The first step comprises the ablation of the uterus and the repair of the anterior vaginal wall by means of nonabsorbable sutures. The second step, which consists of repair of the pelvic floor, is best carried out 2½ to 3 weeks after operation, when the vaginal vault and the anterior vaginal wall have healed. When this method is employed, I usually repair the perineum under local infiltration anesthesia and have also performed the entire operation under the same anesthesia. It is well tolerated by feeble women and by poor surgical risks, since its performance consumes only a few minutes. Its only disadvantage rests in the fact that it requires longer hospitalization than does vaginal hysterectomy by means of sutures. This, however, is frequently advantageous to the patient, since the extra days of rest in the hospital result in noticeable improvement in her general physical condition.

TABLE VI.—ANESTHESIA

	General	Spinal	Local	Para-sacral	Total
Vaginal plastics and abdominal suspension or fixation of uterus	117				117
Interposition operation	178	45		1	224
Vaginal hysterectomy with interposition of broad ligaments	67	56	2		125
Vaginal hysterectomy, clamp method	6	29	1		36
High vaginal fixation of uterus	28	29			57
Manchester operation—Fothergill operation	41	38	6		85
Subtotal colpectomy LeFort operation	12	6	8		26
Total colpectomy	2	3	1		6
Operation for posterior vaginal enterocele	29	24	1		54

High vaginal fixation of the uterus. High vaginal fixation of the uterus in the treatment of uterovaginal prolapse has never been a popular method in the United States, and is but rarely mentioned in the literature. It produces excellent results in first degree and second degree prolapse, and I have found it most helpful in a certain group of cases, such as recurrences after previous vaginal plastics and abdominal fixation of the uterus, these recurrences being difficult to correct because of the tremendous elongation of the uterus in most cases. There were 57 cases in our series. By opening the anterior vaginal wall, separating the bladder from the vagina and uterus and by exerting strong traction on the cervix, it is possible to pick a point on the anterior surface of the uterus corresponding to the highest point in the vaginal incision, just below the urinary meatus. The anterior surface of the uterus at this level is picked up by a suture, the two ends of which are threaded through the vaginal wall on each side and tied; this raises the bladder high in the pelvis. After a high amputation of the redundant cervix, the remainder of the anterior uterine wall is sutured to the vagina by interrupted sutures, and the perineum is repaired. Every recurrence in the class of cases here described, which has come under my observation and treated by this method thus far has given a satisfactory and durable result.

Manchester or Fothergill operation. The Manchester or Fothergill operation is based on uniting the bases of the broad ligaments (cardinal ligaments) in front of the cervix with amputation of this organ when necessary, performing a wide

TABLE VII.—MORTALITY

	Cases	Deaths	Per cent
Vaginal plastics and abdominal suspension or fixation of uterus	117	0	
Interposition operation	224	5	2.2
Vaginal hysterectomy with interposition of broad ligaments	125	5	4.0
Vaginal hysterectomy, clamp method	36	2	5.5
High vaginal fixation of uterus	57	0	
Manchester operation—Fothergill operation	85	0	
Subtotal colpectomy—LeFort operation	26	0	
Total colpectomy	6	0	
Operation for posterior vaginal enterocele	54	1	1.8
Total	730	13	1.7 Gross mortality

TABLE VIII.—CAUSES OF DEATH

Case	Age in years	Cause
		Interposition operation
1	67	Cerebral hemorrhage day after operation
2	52	Diabetic coma 2d day after operation
3	74	Cerebral embolism 8 days after operation
4	73	Acute cardiac dilatation 19 days after operation
5	73	Pulmonary embolism 7 days after operation
		Vaginal hysterectomy with interposition of broad ligaments
1	60	Urinary suppression, uremia; ureters patent by cystoscopy
2	66	Died 72 hours after operation, from uremia. Autopsy showed angulation of ureters by upper suture attaching broad ligaments to upper angle of vagina.
3	64	Died from bronchopneumonia 3d day after operation.
4	66	Died from cerebral hemorrhage, 10th day after operation. Autopsy confirmed diagnosis.
5	56	Died from coronary thrombosis, 13th day after operation.
		Vaginal hysterectomy clamp method
1	43	Died from uremia 5th day after operation. 500 c.c. transfusion before operation. Kidneys never secreted. Cystoscopy. Both ureters patent. Small red contracted kidneys. Nephrostomy right kidney. No urine secreted.
2	53	Died from pulmonary embolism, 25th day after operation. Phlebitis, left leg.
		Operation for posterior vaginal enterocele
1	73	Died from pulmonary embolism, 7th day after operation.

resection of the anterior vaginal wall, plicating the musculofascial tissues attached to the bladder before suturing the anterior vaginal wall, and completing the procedure by a thorough repair of the perineum. In 1903, Aleksandroff published a paper on a method of approximating the broad ligaments in front of the cervix when operating vaginally for uterine prolapse. Twenty-five years ago I was using this principle in an operation which was described in my records as the Aleksandroff operation. In 1933, Fletcher Shaw, read a paper on the Manchester operation before the American Gynecological Society. His presentation popularized this method in America, and it is now done extensively. It is an excellent operation, simple in execution and attended with good results. It is satisfactorily carried out in cases of atrophied uterus. In recent years I have used it in cases in which I should formerly have employed the interposition operation. There were 85 cases in our series.

Subtotal colpectomy. LeFort operation. Subtotal colpectomy, the LeFort operation, is practically devoid of shock especially when done under local infiltration anesthesia. It is useful in older women, at best poor surgical risks, who are afflicted with the total prolapse of a small atrophied uterus, or with inversion of the vagina following supracervical or total hysterectomy. Because of its one disadvantage, namely closure of the vagina, it is applicable only to those women whose ages make sexual relations unimportant. In our series there were 26 cases.

Total colpectomy. Total colpectomy is reserved for the most extensive cases of inversion of the vagina and is employed in old women in whom the marital function may be sacrificed. There were 6 cases in our series.

The efficacy of subtotal and total colpectomy is enhanced by adding a perineorrhaphy. The final result consecutive to the procedure is a small shallow vagina, the union of the levator ani muscles in the median line forming an added barrier against recurrence.

Operation for posterior vaginal enterocele. Following any intervention for prolapse, a recurrence in the posterior vaginal segment is due, in large measure, to the overlooking of a posterior vaginal enterocele, also referred to as a hernia of the cul-de-sac of Douglas, while the perineum is being repaired. In the presence of such a condition, —there were 54 cases in our series—the hernia may roll over a well repaired perineum as the patient gets out of bed after operation, and to all intents and purposes she feels that she has obtained no benefit from the operation. In 1909, Marion of Paris, described posterior vaginal enterocele and advised its correction by opening the abdomen and closing the cul-de-sac of Douglas by means of superimposed pursestring sutures of

nonabsorbable material, care being taken not to include the ureters in these sutures. In 1912, Moschcowitz described a similar but more extensive operation for prolapse of the rectum, this procedure being equally applicable to hernia of the cul-de-sac of Douglas. Finally, in 1922, George Gray Ward proposed a vaginal operation for the radical cure of this disorder. His procedure, carried out entirely through the vagina, consists of mobilizing the cul-de-sac of Douglas on all sides, opening the hernial sac, reducing its contents, ligating its base, and resecting the sac. The uterosacral ligaments are then approximated to each other in their entire length, as a barrier against recurrence, and the pelvic floor is repaired. I have employed the Ward operation in most cases, and have reserved that of Marion and Moschcowitz for very large hernias and those complicated by adhesions.

For the sake of clarity, data regarding the 730 operations for uterovaginal prolapse which I have performed are presented in tables.

RESULTS

All 730 patients in this series were examined as they left the hospital at the end of 2 weeks, and the results were noted. All except those living at far distant points were re-examined at the end of 2 months, and many of them were again examined a year after operation. While it was fairly simple to check the primary results, it was extremely difficult to check the end-results. These operations were performed during a period of 27 years on women coming from the New England states, from states farther distant, and from some of the Canadian provinces. The long distances they had to cover prevented them from returning for subsequent examination. The questionnaire to the family physician or the patient proved to be of little value since in some who claimed good results in the reply letter I found what I should class as fair results on subsequent check-up examination, and again, those who claimed not to have been benefited materially showed excellent anatomical results when seen later. Furthermore, women operated on at a certain time in life may show a good result and 10 or more years later, because of the atrophy of the tissues that has taken place during this time, there may appear descent of the anterior or posterior vaginal wall or of the uterus. Recently two such recurrences were impressive. The first patient was considered to have had a good result for a period of 13 years and 3 months following an interposition operation. Her husband then became severely ill and in caring for him for a period of 8 months it was necessary for her to lift him. She reported after his death, at which time it was found that a small atrophied uterus was completely extruded. This recurrence was corrected by a vaginal hysterectomy with interposition of the broad ligaments, and the result, up to the present time, has been entirely satisfactory. The second patient remained well for 12 years and 4 months after an interposition operation, and then, because of marked atrophy of the uterus and the fact that her occupation necessitated the lifting of heavy weights, a recurrence became apparent. This also has been satisfactorily corrected by vaginal hysterectomy.

The rate of recurrence in all operations for prolapse will no doubt increase with the length of time that the patients are examined. Thus far the following recurrences have been noted in those who have reported for check-up examinations.

Of the group in which vaginal plastics and abdominal suspension or fixation of the uterus was the type of treatment used recurrent cystocele was found 1 year and 3 months after operation in a patient with nulliparous prolapse.

In the interposition group the following results were noted:

Recurrence 6 years after operation—extrusion of cervix—corrected by amputation of cervix, perineorrhaphy, and abdominal fixation of uterus.

Recurrence 2 years and 5 months after operation—atrophy—corrected by right oophorectomy, myomectomy, and abdominal fixation of uterus.

Recurrence 12 years and 4 months after operation—atrophy—corrected by vaginal hysterectomy, and interposition of broad ligaments.

Recurrence 3 years and 8 months after operation—atrophy—patient 73 years of age and refused correction.

Recurrence 10 years and 6 months after operation—atrophy—patient 70 years of age, and refused correction.

Recurrence 6 months after operation—corrected by perineorrhaphy and abdominal fixation of the uterus.

Recurrence 3 years and 3 months after operation—atrophy—corrected by vaginal hysterectomy with interposition of the broad ligaments.

Recurrence 1 month after operation—cervix of an atrophied uterus extruded—corrected by abdominal fixation of the uterus.

Recurrence 8 months after operation. First operation consisted of vaginal plastics and suspension elsehwere; second operation, interposition operation, amputation of cervix and perineorrhaphy.

Recurrence in the form of a posterior vaginal enterocele, corrected by Ward vaginal operation for enterocele.

Recurrence 6 months after operation, corrected by vaginal hysterectomy with interposition of broad ligaments.

Recurrence 1 year and 10 months after operation—atrophy—no correction.

Recurrence 1 year and 1 month after operation. Patient was operated upon in the country. The bladder was allowed to distend up to 32 ounces for a month after operation. Recurrence was in the form of a large cystocele and was corrected by vaginal hysterectomy with interposition of broad ligaments.

In the group in which high vaginal fixation of uterus was done, the following was noted:

Recurrence 2 years and 8 months after operation—large posterior vaginal enterocele—corrected by Ward's vaginal operation for enterocele.

Recurrence, 8 years after operation—in the form of first degree prolapse, due to lifting and straining while moving to another house—was not corrected.

Recurrence 3 years and 4 months after operation—very small atrophied uterus; cervix extruded on straining—corrected by vaginal hysterectomy with interposition of broad ligaments and Ward vaginal operation for enterocele; perineorrhaphy.

Recurrence 4 months after operation—cervix extruded on straining—not corrected. Amputation of cervix was advised, but was refused.

Of the group in which the Manchester operation (Fothergill operation) was used the recurrences were as follows:

Recurrent cystocele noted a few months following operation—patient 68 years of age, and refused a second operation.

Recurrence 1 year and 4 months after operation—medium posterior vaginal enterocele—corrected by Ward vaginal operation for enterocele.

Recurrence 1 year and 7 months after operation—small cystocele—not corrected.

In the subtotal colpectomy. (LeFort operation) group there was 1 recurrence:

Recurrence 3 months after operation—cervix appeared at vulva—there were thin, atrophic tissues with poor blood supply and imperfect healing.

In the total colpectomy group there were no recurrences observed thus far.

In the group having operation for posterior vaginal enterocele, the following was noted:

Recurrence a few months after operation—slight bulging of cul-de-sac of Douglas on straining after the Moschcowitz operation for enormous hernia. No correction was necessary.

Recurrence a few months after operation—slight bulging of the cul-de-sac of Douglas after the Moschcowitz operation for a large enterocele. No correction was necessary.

In 1 case separation of the skin of the perineum due to poor blood supply of tissues was corrected by the edges being freshened and approximated with prepared silk. Good healing

CONCLUSIONS

Uterovaginal prolapse in young women during the childbearing age may be satisfactorily treated by repairing the cervix, the anterior and posterior vaginal walls and the perineum, by shortening the uterosacral ligaments, and by performing a round ligament suspension of the uterus.

After the menopause one of the vaginal methods is given the preference because of increased operability, on account of lessened morbidity and mortality. An abdominal incision is made only in a very limited number of cases to correct a recurrence and to obliterate a very large posterior vaginal hernia.

The interposition operation (Watkins-Schauta-Wertheim) followed by amputation of the cervix gives excellent results in properly selected cases, and this operation has been used in the largest number of cases in this series.

Vaginal hysterectomy with interposition of the united broad ligaments is reserved for women with atrophied uteri and in whom cancer is present or suspected.

Vaginal hysterectomy, clamp method, is ideal in old women when hysterectomy is indicated and when the time element is a factor.

High vaginal fixation of the uterus with amputation of the cervix is useful in the first and second degrees of prolapse, with a large cystocele, and when recurrence has occurred subsequent to an abdominal fixation of the uterus.

The Manchester or Fothergill operation in recent years has supplanted the interposition operation and vaginal hysterectomy in a number of cases. Its technique is simple and its results uniformly satisfactory. It has the advantage of being a surface operation since the peritoneal cavity is not entered.

In worn out and feeble old women, in whom an extensive vaginal operation is contraindicated, subtotal colpectomy (LeFort operation) or total colpectomy, especially when performed under local anesthesia, may render great service.

One or the other method of colpectomy may be used to advantage in inversion of the vagina following supracervical or total hysterectomy.

A posterior vaginal enterocele (hernia of the cul-de-sac of Douglas) which not infrequently accompanies uterovaginal prolapse should receive adequate surgical treatment.

An adequate repair of the pelvic floor is essential in all cases, with the rare exception of women with nulliparous prolapse in whom the perineum is intact and gives good support.

The vaginal methods, because of the minimum amount of postoperative shock and the comfortable convalescence which follows, are ideal operations in older women.

Local and spinal anesthesia may be used advantageously in a number of patients.

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SO CALLED "ASEPTIC OR CHEMICAL MENINGITIS"

Report of Two Cases

H. LIVINGSTONE, M.D., V. WELLMAN, M.D., D. CLARK, M.D., and V. LAMBROS, M.D.,
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THE incidence of so called "aseptic meningitis" following lumbar puncture or spinal anesthesia is comparatively rare; however, we believe that the condition is overlooked in some patients who, particularly during the first four postoperative days, do not receive very close medical supervision, by a person cognizant of this complication. Diagnosis of this condition should be made promptly and treatment instituted immediately in order to obtain quick relief from distressing symptoms. Orkin in a summary of 45,966 cases of spinal anesthesia reported by 20 authors, gives an incidence of 0.26 per cent of aseptic meningitis.

It is known that this complication can follow simple lumbar puncture. Spiller and Payne reported aseptic meningitis following lumbar puncture in an epileptic. Reynolds and Wilson reported three such complications following lumbar punctures on patients on whom previous diagnoses of cerebral syphilis, chronic encephalitis, and frontal tumor, respectively, had been made. The symptoms and findings were fever, stiff neck, positive Kernig's sign, stupor, and delirium. A pronounced increase in the cells in the spinal fluid was found without organisms being demonstrable by smear or culture, and without reduction in the amount of sugar in the spinal fluid.

Zahradicky, Dijon, Arnheim and Mage, and Hyslop have each reported one case of aseptic meningitis following spinal anesthesia, and Campbell, as well as Brock, Bell, and Davison, have reported 2 cases. As can be seen in Table I allocain, neocaine, nupercaine, novocain, and procaine with strychnine or adrenalin were the chemical agents employed.

Seven of these 8 cases appearing in Table I were reported in detail. The time of onset of symptoms varied from almost immediately after surgery to 60 hours after operation. Some or all of the following symptoms were observed in these 7 patients: headache, fever, pain or rigidity of the neck, semicoma or coma, malaise and anorexia, vomiting, haziness of the optic discs, increased pulse rate, overactive knee jerk, positive Babinski signs, unilateral or bilateral Kernig, and absent knee jerks and lower abdominal reflexes.

Lumbar puncture revealed turbid spinal fluid which, upon microscopic examination, presented a lymphocytosis, pleocytosis of polymorphonuclear leucocytes, or a monocytosis, with no organisms being demonstrable. Four patients recovered by the 5th to the 22d postoperative days, while 3 succumbed on the 20th, 21st and 30th postoperative days, respectively.

We wish to present 2 instances of chemical meningitis following spinal anesthesia.

REPORT OF CASES

CASE 1. A male university student, aged 20 years, in excellent general condition and weighing 65 kilograms, had a left inguinal herniotomy performed under spinal anesthesia on November 7, 1941. He received morphine sulfate 0.010 gram (hypodermically) 1 hour before surgery, and ephedrine sulfate 0.049 gram (hypodermically) immediately before the lumbar puncture which was performed readily and without incident. There was no apparent trauma or hemorrhage. One hundred and fifty milligrams of novocain crystals dissolved in 4 cubic centimeters of clear spinal fluid was injected in the third lumbar interspace. Anesthesia to pin-prick was present to the 8th dorsal bilaterally 8 minutes after injection. Blood pressure, pulse, color, and respiration remained unchanged, and the patient was comfortable and co-operative throughout surgery which lasted 1 hour and 45 minutes. There was still some anesthesia present when the patient left the operating room.

Fourteen hours after operation he developed a throbbing headache which originated in the occipital region and radiated forward bilaterally. Accompanying this were nausea, vomiting, and photophobia. Twenty-four hours after operation the temperature was 102 degrees. The only neurological abnormality was a cervical rigidity. Lumbar puncture revealed cloudy spinal fluid, with a pressure of 170 millimeters of cerebrospinal fluid with normal dynamics. There was a marked increase in cells, particularly lymphocytes, in the spinal fluid. Other laboratory findings are presented in Table II.

The headache was relieved by daily lumbar punctures with removal of spinal fluid, and had disappeared by the 2d postoperative day. Although there was no muscle tenderness the stiffness of the neck persisted until the 3d postoperative day. By the 4th postoperative day the patient was very comfortable and symptomless and was discharged apparently completely recovered one week later.

CASE 2. A 28 year old female, weighing 43.6 kilograms, entered the hospital with a history of having had an old gonococcic infection of the pelvis which had been treated

From the Department of Surgery of the University of Chicago.

TABLE I.—REPORTED CASES OF ASEPTIC MENINGITIS

Authors	Cases after lumbar puncture only	Cases after spinal anesthesia	Agent	Time of onset after operation	Clinical course	Outcome
Spiller and Payne	1					
Reynolds and Wilson	3					
Zahradicky		1	Procaine and adrenalin	Soon	Headache, fever, neck pain	*Recovery*, 14th day
Dijon		1	Allocain		48 polymorphonuclear leucocytes	*Death*, 20th day, No autopsy
Arnheim and Mage		1	Neocaine		No details given	
Hyslop		1	Neocaine	60 hrs.	Increased spinal fluid pressure, 480 cells with 90% lymphocytes. Stupor and stiff neck	*Recovery*
Campbell		1	Nupercaine	8 hrs.	Headache, vomiting, fever, 2000 cells with 80% polys, 18% small monos and 2% large monos. Had repeated cisternal punctures with antimeningococcic serum injected	*Death*, 30th day. Autopsy, monocytic meningitis—etiology undetermined
		1	Novocain	17 hrs.	Headache, fever. 5400 cells with 90% polys to 3,920 cells with 91% polys, 4% small monos, 3% large monos, and 2% transitional, trace globulin and 1+ sugar. Recovered and discharged on 7th p.o. day. Sudden onset of coma and death on 21st day	*Death*, 21st day. Autopsy, acute purulent meningitis. Etiology undetermined
Brock, Bell and Davison		1	Procaine and strychnine	Soon	Spinal fluid contained lymphocytes, mononucleosis beginning with 560 cells. Symptoms gradually increased in severity, and decreased by lysis	*Recovery*, 22nd day
		1	Nupercaine	3 hrs.	Coma. Polynucleosis of 3,200 cells and disappearance of spinal fluid sugar	*Recovery*, 5th day

preceding a partial hysterectomy performed elsewhere in 1933. On admission she presented a right lower abdominal mass, but otherwise was in good general condition. On November 12, 1941, an exploratory laparotomy and right oophorectomy were performed under spinal anesthesia. Morphine sulfate 0.010 gram (hypodermically) was administered 1 hour before the patient came to surgery. Ephedrine sulfate 0.049 gram (hypodermically) was given just before the lumbar puncture which was made in a rapid and uneventful manner at the third lumbar interspace. One hundred and forty milligrams of novocain crystals (from a 150 mgm. ampul) dissolved in 4 cubic centimeters of clear spinal fluid was injected. Ten minutes later anesthesia to pinprick was present to the 6th dorsal bilaterally. The operation consumed 1 hour and 5 minutes, and the anesthesia was very uneventful throughout.

Fourteen hours after surgery the patient developed a severe, throbbing headache which was generalized, nausea, bilateral tinnitus which was more intense in the left ear, and photophobia. Eight hours later the temperature was 101 degrees. At this time the only neurological finding was a cervical rigidity. Lumbar puncture revealed the spinal fluid to be of ground glass appearance with a cell count of 9,600 per cubic millimeter consisting of 99 per cent lymphocytes and 1 per cent polymorphonuclear leucocytes. Other findings, including chemical and microscopic examination of the spinal fluid obtained by repeated daily spinal punctures, appear in Table II. There was a gradual decrease in the symptoms and on the 5th postoperative day the cervical rigidity had disappeared. The course thereafter was uneventful, and on the 14th postoperative day the patient was discharged in good condition.

We have made careful postoperative observations in a series of approximately 4,000 cases of

TABLE II.

Case and dates	Total Protein mgm. %	Chlorides M/L	Sugar mgm. %	Total cell count	%Lymphocytes	%Polymorphonuclears	Appearance	Initial pressure mm.
Case 1— Operation on 11-7-41								
11-8-41	180	118.3		4000	99	1	Ground glass	170
11-9-41	58.8	118.3		552	90	10	Rapidly clearing	70
11-10-41	53.7	119.5	42	69	96	4	Clear	130
11-11-41	28.1	123.1		5	100	0	Clear	100
Case 2— Operation on 11-12-41								
11-13-41	221	119.5	46	9600	99	1	Ground glass	155
11-14-41	20	125.8	60	2200	95	5	Clear	150
11-15-41	231	126		103	94	6	Clear	

Pandy negative in both cases.
Culture showed, in both cases, no growth on any media, including brain.

spinal anesthesias. Previously over 2,500 spinal anesthesias had been administered without observing this complication. A different and experienced anesthetist administered the procaine to each patient. The same careful technique was employed throughout the series as to the sterilization of equipment and the method of administration. Lumbar puncture was readily and uneventfully performed in each instance. Both patients received novocain from 150 milligram ampuls and the drug, in a crystal form, was mixed with 3.5 to 4 cubic centimeters of clear spinal fluid before injection.

It is of interest that in the 2 patients presented in Table II there was an initial marked postoperative increase in the total protein content of the spinal fluid above the normal level of 30 milligrams per 100 cubic centimeters. There was an accompanying slight drop in the spinal fluid chlorides initially, but this followed the protein in returning to a normal level in a few days.

In each subject there was a marked increase in the total cell count on lumbar puncture made 24 to 36 hours after operation. Lumbar puncture revealed cloudy spinal fluid with an increase in lymphocytes in our patients, and polymorphonuclear leucocytes, lymphocytes or monocytes in previously reported cases. Culture of the spinal fluid from our patients showed no growth on any media. An unsuccessful search was also made for a virus by injecting the spinal fluid subcutaneously in the foot pads of guinea pigs and intracerebrally and intraperitoneally in mice. The distressing symptoms of headache and pain on movement of the head were relieved in our patients by daily lumbar puncture and removal of 20 cubic centimeters of spinal fluid. This procedure also brought about a rapid decrease in the cell constituents, with the total protein and chloride content of the spinal fluid returning to normal levels. Our patients made prompt recoveries.

SUMMARY

Two cases of chemical meningitis following novocain spinal anesthesia are reported, and 8 additional cases following various spinal anesthetic agents are collected from other authors and reviewed. Four cases following simple lumbar puncture are reported which were taken from the literature.

Our patients recovered promptly after daily lumbar puncture and removal of spinal fluid. Of the 8 previously reported cases following spinal anesthesia 4 recovered and 3 died. The outcome was unknown in 1 instance. The 4 following simple lumbar puncture recovered from their meningitic symptoms.

It appears that chemical meningitis is an infrequent complication of spinal anesthesia, yet it behooves every surgeon and anesthetist to be cognizant of this rare complication and to see that the correct diagnosis is made and adequate therapy instituted. Apparently the incidence of this hazard is so infrequent that it should not deter the experienced anesthetist from employing this method of anesthesia when, after adequate consideration, it appears to be indicated.

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EDITORIALS

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PLEURAL EMPYEMA

SINCE the principles of treatment that produce a high percentage of cure of empyema are not being widely applied in civilian practice and since war injuries of the chest so frequently result in empyema, a consideration of the modern management of this disease is timely. In spite of the best early management of war wounds involving the thoracic cavity and in spite of the early use of the sulfonamides, many deaths and a great aggregation of chronically disabled soldiers will occur during and after this, as after the last, war unless the cases of empyema are properly managed.

The frightful mortality of empyema during the influenza epidemic of twenty-six years ago led to the investigations and invaluable recommendations of the Empyema Commission of the Surgeon General of the United States Army, of which Dr. Evarts A. Graham was the chairman. Essentially, these recommendations were that an acute empyema should not be surgically drained until pleural adhesions at the limits of the empyema cavity have become sufficiently firm to prevent collapse of the lung at the time a drainage tube is introduced. It was found that the pleural adhesions are sufficiently firm when the aspirated pleural fluid shows a sediment of approximately 75 to 90 per cent of pus after standing overnight. While the formation of firm adhesions is awaited the size of the empyema and the degree of toxic absorption from the pus should be reduced by partial aspiration of the pleural fluid every one or, at most, every two days. Air should never be injected into a nontuberculous empyema because this prevents the progressive expansion of the lung and because the rise of air to the upper part of the pleural cavity actually creates an empyema space there. Surgical drainage should not be delayed beyond the recommended time since progressive fibrosis in the pulmonary and diaphragmatic walls of the empyema cavity delays, or may even prevent, obliteration of the empyema cavity by expansion of the lung and elevation of the diaphragm.

If it is assumed that surgical drainage is carried out neither too soon nor too late, the manner in which drainage is accomplished and continued will, in many cases, determine whether the empyema will heal promptly or whether it will remain as a cause of prolonged disability.

Dependent air-tight drainage is of prime importance. Since obliteration of the costophrenic sinus by adhesions occurs in varying degree, the floor of the empyema cavity rarely corresponds with the floor of the normal pleural cavity and, therefore, no given rib

represents the proper site for drainage in every case. The simplest way of determining the position of the floor is to aspirate from below upward in successive intercostal spaces until pus is found. In the horizontal direction, the scapular or paravertebral line is the most dependent site for drainage while the patient is lying upon his back, but he will not lie upon his back when a drainage tube is pressed against the incision by the mattress. The posterior axillary line just free of the mattress is, therefore, the site of election for the insertion of drainage.

Intercostal drainage with a catheter or any small-bore tube is an inefficient type of drainage. The small lumen of such tubes frequently becomes occluded by masses of fibrin and pus, with the result that drainage of the empyema pus is obstructed. The pus then leaks out around the tube and air is sucked in around the tube, air-tight suction drainage thereby being lost. The use of a thumb-sized tube after the resection of a six centimeter length of a rib produces continuous drainage that will remain air-tight indefinitely, provided that the incision in the deep layer of the periosteum and underlying parietal pleura is only long enough to permit the snug introduction of the tube. The incision in the extracostal muscles need not be sutured, and the incision in the skin should not be. The tube should not be fenestrated; its inner beveled end should be placed just within the pleural cavity with the opening of the tube facing away from the diaphragm. If the tube is introduced too far, pus will collect in the bottom of the empyema, and if the end of the tube does not reach the pleural cavity, the tissues of the thoracic wall will gradually contract over the end of the tube and obstruct drainage.

The outer end of the long drainage tube should be put under water in a jar placed on the floor. The evacuation of pus and air from the empyema cavity creates a negative pressure in the cavity which tends constantly to expand the lung, elevate the diaphragm, and obliterate the cavity. In cases in which expansion is unduly delayed, the negative pressure in the drainage system can be greatly increased by some form of mechanical suction apparatus, the pressure of which is regulated by the introduction of an open tube for a variable distance beneath water in a control bottle. Such highly negative pressure drainage often cures a chronic empyema for which a Schede thoracoplasty would otherwise be necessary.

A final matter of great importance in the avoidance of a chronic empyema is the maintenance of the drainage tube in the entire thickness of the thoracic wall until the empyema cavity has become completely obliterated; only then should the tube be periodically shortened as the drainage track fills in from the bottom. The decreasing size of the cavity may be measured from time to time by the instillation of measured amounts of fluid, by exploration of the limits of the cavity with a uterine sound or, if the residual cavity is small, by palpation with a finger; when the cavity is represented by only a narrow and perhaps sinuous track, the instillation of iodized oil, followed by the making of x-ray films, best reveals the extent of the empyema. When an empyema that has not already become chronic holds only thirty cubic centimeters of fluid, negative pressure drainage may be dispensed with by cutting off the tube close to the skin.

Shell wounds of the thorax involving the pleural cavity and particularly the lung, frequently result in empyema. When such wounds produce a sucking pneumothorax requiring débridement and closure of the opening in the thoracic wall by suture of the extra-

costal muscles, the vital integrity of the suture line is safeguarded by immediate air-tight, water-seal, dependent drainage of the pleural cavity. Such drainage has the additional important advantage of removing air that escapes from a wound of the lung, thereby preventing a tension pneumothorax. The constant drainage of fluid produced by the trauma decreases the chance of the development of an extensive empyema and, if one does form, its severity will be lessened by the drainage that has already been instituted, and by early expansion of the collapsed lung.

JOHN ALEXANDER.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

IT is a great pleasure to review the new edition of Dr. Curtis's book *A Textbook of Gynecology*.[1] It can be stated without equivocation that it is the most satisfactory of all modern texts on Gynecology. Compact, clear, concise, and beautifully illustrated, it is indispensable to the practitioner, the gynecologist, and to the surgeon doing gynecology. The text is very comprehensive and all subjects of importance are complete.

The illustrations are superb and the drawings of the pelvic fascias and muscle compartments, always a puzzle to medical students and more so to practicing gynecologists, are unique. For teachers the pelvic drawings and descriptions are invaluable. The illustration of the various somatic and sympathetic nerves, and the demonstration of the course of blood vessels should give each student many thoughtful hours of study. Dr. Curtis, his assistants, and the artist—Tom Jones—have demonstrated to all of us many valuable lessons in the art of dissecting, of description, and of illustration.

In such a book a few things should be criticized. I believe that although the drawings of the radical hysterectomy are clear and well done, the operation as described has little value. For simple total abdominal hysterectomy it is too radical; for cancer of the endometrium, if one is to be radical, it is not radical enough and it is not nearly as extensive as it should be for the present conception of the Wertheim-Clark procedure. The latter operation will be done more and more in the near future and illustrations and descriptions of the dissection of the large vessels and the obturator fossae should be presented.

There is no mention of the importance of venograms and ligations of the deep and superficial femoral veins, or the external iliac veins in thrombophlebitis, or in patients with embolism. It is my impression that in a treatise on gynecology the chapters on preoperative and postoperative care, except as it explicitly applies to the gynecologic patient, should be omitted. Inasmuch as gynecologic surgery is surgery, it is better that descriptions of the care of the patient be left to general surgical authors and that references to their works be sufficient for a text of gynecology.

But for these few criticisms, and they are minor ones, this book is exceptional, and in the opinion of the reviewer Dr. Curtis's book can be considered one of the important small volumes on this specialty.

JOE V. MEIGS.

[1] A TEXTBOOK OF GYNECOLOGY. By Arthur Hale Curtis, M.D. 4th ed. Philadelphia and London: W. B. Saunders Co., 1942.

THE new text, *Synopsis of Pathology*[2] by W. A. D. Anderson, is a useful addition to the already numerous but not always adequate textbooks written for the student of medicine. In his preface the author states that it was "intended to fill a gap which has existed between the very elementary manuals of pathology and the abundant excellent larger textbooks and reference works." The book is remarkable for the fact that in so much of its content it is strictly up to date. The bibliography which follows each chapter is brief, well selected, and most of the references are of recent date.

In its arrangement, the conventional pattern is followed. In the first 11 chapters the author discusses the subjects usually included in a section on general pathology. Among these are included a chapter on virus and rickettsial diseases and a brief chapter each on chemical poisons and vitamin deficiencies. In the remaining 14 chapters, disease processes are discussed by systems, i.e., cardiovascular system, kidneys, urinary tract and male genitalia, the lungs, etc. In the paragraphs on subjects which are more important from the clinical standpoint, all essential data are included in abbreviated form but theoretical considerations, historical facts, and "medical mythology" are largely missing. Many short paragraphs with definitions and brief explanatory notes on the subjects of less importance or of rare occurrence are included.

The section on endocrine glands, while brief (37 pages and 26 illustrations), is especially well written and to the point. The chapter which follows it on female genital organs is likewise excellent for the purposes of the medical student.

Illustrations are numerous (294 text illustrations and 17 color plates in 638 pages of text). The photomicrographs are generally good but many of the photographs of gross material are technically of poor quality. More than one-half of the color plates are excellent.

This interesting, readable volume in pocket size should be attractive and useful to the medical student, interne, or practitioner of medicine or surgery who wishes to refresh his memory and bring his concepts of disease processes in line with recently acquired knowledge.

F. D. GUNN.

THE material presented in *The Sexual Glands of the Male*[3] has been assembled from the work of

[2] SYNOPSIS OF PATHOLOGY. By W. A. D. Anderson, M.A., M.D. St. Louis: The C. V. Mosby Co., 1942.

[3] THE SEXUAL GLANDS OF THE MALE. By Oswald Swinney Lowsley, A.B., M.D., F.A.C.S., in collaboration with Frank Hinman, Donald R. Smith and Robert Gutierrez. (Reprinted from Oxford Loose-Leaf Urology.) New York, London, Toronto: Oxford University Press, 1942.

several contributors to the *Oxford Loose-Leaf Urology* under the editorship of Dr. Lowsley.

Lowsley's chapters on the prostate gland cover most completely, but concisely, the embryology, anatomy, pathology, symptomatology, diagnosis and treatment—both surgical and medical. The discussion on embryology and anatomy is authoritative since the author has himself contributed much of the accepted information on these subjects. Modern concepts as to the etiology of prostatic hyperplasia and the added rôle of associated endocrine changes is well presented. The rôle of castration and the inhibitory effects of estrogen therapy on carcinoma of the prostate are adequately, but briefly, presented since this important subject is still in the stage of clarification.

Hinman and Smith have contributed an excellent survey of the embryology, anatomy, and physiology of the testes and epididymides. Diseases of these structures are considered in detail. The discussion on tumors of the testicle is most noteworthy as it brings up to date a subject in which the authors have made many contributions during the past 20 years.

The chapter of Gutierrez on the seminal vesicles, ampullae, vasa deferentia, and spermatic cord is a most exhaustive compilation of conditions which are only briefly discussed in most texts on surgery and urology.

Excellent illustrations by William P. Didusch add greatly to the value of the text.

This work can be heartily recommended to those who are especially interested in the sexual glands of the male. VINCENT J. O'CONOR.

THE small volume by R. D. Langdale-Kelham[1] on amputations and artificial limbs satisfies a real need in the armed forces and in the civilian doctor population because it deals adequately with the principles which underlie these subjects. The book contains less than a hundred small pages, but it holds all that a man in general practice need know upon the subject. Its organization of material brings out the important points with well defined clarity.

The main issues in amputations are not confused by irrelevant details. However, few details of any importance have been left out. The text is clear and readable. The illustrations of the operations and of the prostheses are line drawings which are simple but are well made. Their simplicity makes for easy recognition of the points that the drawings are intended to stress. Particularly is this true of the drawings which deal with the artificial limbs. The legends and sublegends are clear, and the captions on the drawings are fully explanatory. It is evident throughout that there has been full co-operation between the limb surgeon and the limb maker.

The authors very wisely have omitted any consideration of the specially named amputations, such as the Syme, Gritti-Stokes, Pirogoff, and so on. These operations have been outmoded, largely because of advances made in the limb makers' art.

Only the three major elective amputations in the upper and in the lower extremities have been described. However, many clinical features common to all amputations have been dealt with. The anatomy involved has been treated physiologically. Disarticulations have not been mentioned.

C. LATIMER CALLANDER.

THE general practitioner to whom the volume *Indigestion, its Diagnosis and Management*[2] by Rehfuss is dedicated will profit greatly by the recorded precepts of this student of gastroenterology. Dr. Rehfuss presents his thoughts on indigestion in an orderly fashion and by an attractive conversational method as might be used in clinical teaching. The term indigestion as used by the patient has been broken to a workable etiological basis and then the discussion of the several entities follows.

There are 29 chapters, two-thirds of which are devoted to a discussion of these separate entities. Dr. Philip Hawk contributed the chapters on vitamins and water metabolism. The chapters on history taking and examination of the patients, gastritis, peptic ulcer, and enteritis are excellent and could be read with profit not only by the general practitioner but by the undergraduate student of medicine. A substantial amount of space has been devoted to hepatobiliary disease thus giving the necessary emphasis to this very important subject.

There seems to be an overemphasis given to the details pertaining to food stuffs and not enough discussion to the why and wherefore of everyday practical diets. Furthermore, if this is a book for the general practitioner why the lengthy discussion in methods and technique of gastroscopy and roentgenology? The author's rules on feeding in carcinoma of the stomach and pancreatic disease and his "dietary precepts" are well presented and add greatly to the value of the book.

The organization and presentation of the material in this book reveal the independent thinking of a physician well grounded in research and clinical experience. LOWELL D. SNORF.

THE present war time need for knowledge of the subject of jaw and facial bone fractures makes the book written by Major and his collaborators[3] a timely contribution.

Well arranged, this book opens with a general discussion of fractures which is very complete, and it is gratifying to find stress placed upon the desirability of conservation in dealing with bone fragments, with consequent better results and lessened deformity. Diagnosis is ably presented and the ma-

[1] AMPUTATIONS AND ARTIFICIAL LIMBS. By R. D. Langdale-Kelham, M.R.C.S., L.R.C.P., and George Perkins (MC), F.R.C.S. General editor, The Rt. Hon. Lord Horder, G.C.V.O. London: Humphrey Milford (Oxford University Press), 1942

[2] INDIGESTION, ITS DIAGNOSIS AND MANAGEMENT; WITH SPECIAL REFERENCE TO DIET. By Martin E. Rehfuss, M.D. Philadelphia and London: W. B. Saunders Co., 1943.

[3] FRACTURES OF THE JAWS AND OTHER FACIAL BONES. By Glenn Major, B.S., A.M.(Path.), M.S.(Exper. Surg.), Ph.D.(Surg.), D.D.S., M.D., F.A.C.S. St. Louis: The C. V. Mosby Co., 1943.

terial on the displacement of fragments is much more complete in detail than is usual, and anatomical drawings supplement the text.

Emergency treatment includes the neurological aspects of facial injuries and some exceedingly good advice is offered the general surgeon and the oral surgeon, relative to brain injury and shock.

The discussion of the various methods of inducing anesthesia leaves nothing to be desired.

The author, rightly, devotes considerable space to treatment. There is no departure from accepted procedures in reduction, or immobilization and fixation, but there is free discussion based upon sound pathological and physiological principles.

There is an expressed belief that the method used must be adapted to the case, and a great number of different approaches have been described and illustrated.

The criticism of some of the methods has been reasonable and generous. It is interesting to note that the use of extraoral fixation by means of screws and pins placed and held in fragments finds no enthusiastic endorsement.

A commendable feature of this book is the unusual attention paid to postoperative care and to complications. Too often these matters are treated perfunctorily.

Radiographic examination and the technique employed is presented in a simple and useful manner by one who understands the difficulties encountered in this field.

The discussion of war aspects of jaw fractures emphasizes the essential difference between civil and military practice.

This book is well written, concise, and eminently practical; the subject matter is calculated to be of great interest and value to both physician and dentist, and to stimulate a desirable understanding and co-operation in the care and treatment of these fractures. FREDERICK W. MERRIFIELD.

THE book *Endoscopic Prostatic Surgery* by Roger W. Barnes,[1] is a 224 page monograph with 104 illustrations on a subject which could only be properly handled by a man with large clinical experience.

This is a timely discussion and among the first, as the procedure has not been in general use long enough to have an adequate discussion in all its aspects in one publication. It has a real purpose to fulfill in supplementing those residents and younger urologists who are in the process of developing endoscopic prostatic technique. There is no substitute for actual experience but a simple discussion, as herein presented, of all phases of this procedure makes it a very valuable one for those especially in their developing stages.

There is a chapter on the pertinent anatomical points connected with endoscopic surgery and attention is directed to the necessity of being a competent and experienced cystoscopist before any attempt is made to become a resectionist and this includes, obviously a complete understanding and recognition, cystoscopically, of the various anatomical structures involved.

A well organized discussion on prostatism is presented with his personal indications and contraindications for surgical management for each type.

The routine examination of the patient with prostatism is taken up in great detail and could well serve as a guide for those not entirely familiar with this phase of prostatic surgery.

The author wisely states that his indications for resection may not be the same as for all other surgeons, as this phase of the work must vary with each individual surgeon, but there is presented a full discussion of this subject which is fundamental and thorough. Work of this kind would not be complete without a thorough discussion of the preoperative management of patients with prostatism as well as the meticulous care and detail necessary for their proper management after resection. A complete discussion of the various anesthetics available for this operation is completely and sensibly discussed.

There is enough history of the procedure in the work, as well as the development of various instruments in perfecting the procedure, to satisfy academic interest although this has not been carried to the boring stage.

Without much doubt the section on actual technique with accompanying illustrations will be very helpful to those developing technique and gaining experience and could be used with value by many others presumed to have developed a technique. The author is to be congratulated upon an honest discussion of the various pitfalls of the procedure and the complications resulting not infrequently from endoscopic prostatic surgery. This chapter alone, in conjunction with postoperative care, could be carefully scrutinized with benefit by any urological surgeon regardless of his experience.

This is a very timely monograph, well organized, simply presented, and should have a real place in the development of younger men in the field of endoscopic prostatic surgery. HARRY CULVER.

[1] ENDOSCOPIC PROSTATIC SURGERY. By Roger W. Barnes, M.S., M.D., F.A.C.S. St. Louis: The C. V. Mosby Co., 1943.